

REFORMING THE DRUG COMPOUNDING REGULATORY FRAMEWORK

HEARING BEFORE THE SUBCOMMITTEE ON HEALTH OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED THIRTEENTH CONGRESS FIRST SESSION

JULY 16, 2013

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REFORMING THE DRUG COMPOUNDING REGULATORY FRAMEWORK

TUESDAY, JULY 16, 2013

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 3:05 p.m., in room 2322, Rayburn House Office Building, Hon. Joseph R. Pitts (chairman of the subcommittee) presiding.

Present: Representatives Pitts, Burgess, Shimkus, Murphy, Blackburn, Lance, Griffith, Bilirakis, Ellmers, Dingell, Schakowsky, Green, Barrow, Christensen, Castor, and Waxman (ex officio).

Staff Present: Clay Alspach, Chief Counsel, Health; Sean Bonyun, Communications Director; Noelle Clemente, Press Secretary; Paul Edattel, Professional Staff Member, Health; Julie Goon, Health Policy Advisor; Sydne Harwick, Legislative Clerk; Carly McWilliams, Professional Staff Member, Health; Andrew Powaleny, Deputy Press Secretary; Chris Sarley, Policy Coordinator, Environment and Economy; Heidi Stirrup, Health Policy Coordinator; John Stone, Counsel, Oversight; Alli Corr, Minority Policy Analyst; Eric Flamm, Minority FDA Detailee; Elizabeth Letter, Minority Assistant Press Secretary; Karen Lightfoot, Minority Communications Director and Senior Policy Advisor; Karen Nelson, Minority Deputy Committee Staff Director for Health; and Rachel Sher, Minority Senior Counsel.

OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. PITTS. The time of 3 o'clock having arrived, we will call the meeting of the subcommittee to order.

The chair will recognize himself for an opening statement.

As we all know, in the summer and fall of 2012, a Massachusetts company, the New England Compounding Center, NECC, shipped over 17,000 vials of an injectable steroid solution from three contaminated lots to healthcare facilities across the country. And after receiving injections of NECC's contaminated steroid, over 50 people died from complications associated with fungal meningitis and 700 others were stricken with meningitis and other persistent fungal infections. The outbreak ranks as one of the worst public health crises associated with contaminated drugs in the history of the United States.

Shortly after the contamination came to light, the committee began an investigation into the matter, requesting documents from the Food and Drug Administration and the Massachusetts Department of Public Health, examining whether the outbreak could have been prevented and reviewing existing Federal and State regulatory authority over compounding pharmacies acting as manufacturers.

Both this subcommittee and the Oversight and Investigations Subcommittee have held multiple hearings on the issues surrounding compounded drugs. Today's witnesses are here to discuss three legislative proposals released since the outbreak, including a discussion draft authored by my colleague, Morgan Griffith.

[The discussion draft follows:]

113TH CONGRESS
1ST SESSION

H. R. _____

To amend section 503A of the Federal Food, Drug, and Cosmetic Act with
respect to pharmacy compounding.

IN THE HOUSE OF REPRESENTATIVES

Mr. GRIFFITH of Virginia introduced the following bill; which was referred to
the Committee on _____

A BILL

To amend section 503A of the Federal Food, Drug, and
Cosmetic Act with respect to pharmacy compounding.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Compounding Clarity
5 Act of 2013”.

6 **SEC. 2. PHARMACY COMPOUNDING.**

7 Section 503A of the Federal Food, Drug, and Cos-
8 metic Act (21 U.S.C. 353a) is amended to read as follows:

1 **“SEC. 503A. PHARMACY COMPOUNDING.**

2 “(a) IN GENERAL.—Sections 501(a)(2)(B),
3 502(f)(1), and 505 shall not apply to a drug product for
4 human use if each of the following conditions is met:

5 “(1) IDENTIFIED PATIENT AND RECEIPT OF
6 PRESCRIPTION.—The drug product is compounded
7 for an identified individual patient based on the re-
8 ceipt of a valid prescription order, approved by the
9 prescribing practitioner, stating that a compounded
10 product is necessary for the identified patient.

11 “(2) TIMING AND SPECIFICITY OF PRESCRIP-
12 TION OR PURCHASE ORDER.—The compounding of
13 the drug product is performed—

14 “(A) by a licensed pharmacist in a State-
15 licensed pharmacy or a Federal facility, or by a
16 licensed physician, on the prescription order for
17 such individual patient made by a licensed phy-
18 sician or other licensed practitioner authorized
19 by State law to compound and prescribe drugs;

20 “(B) by a licensed pharmacist or licensed
21 physician in limited quantities before (notwith-
22 standing paragraph (1)) the receipt of a valid
23 prescription order for such individual patient
24 when—

25 “(i) the licensed pharmacist or li-
26 censed physician has historically received

1 valid prescription orders for the
2 compounding of the drug product; and

3 “(ii) the orders have been generated
4 solely within an established relationship be-
5 tween the licensed pharmacist or licensed
6 physician and—

7 “(I) such individual patient; or

8 “(II) the physician or other li-
9 censed practitioner who will write
10 such prescription order; or

11 “(C) by a licensed pharmacist or licensed
12 physician pursuant to a non-patient-specific
13 purchase order (notwithstanding paragraph (1))
14 submitted by a health care provider, which pur-
15 chase order provides assurances that—

16 “(i) the drug product will be adminis-
17 tered by a health care practitioner within
18 a physician’s office, a hospital, or another
19 health care setting; and

20 “(ii) patient-specific valid prescription
21 orders—

22 “(I) will be submitted, electroni-
23 cally or otherwise, to the pharmacist
24 or physician not later than 7 days

4

1 after the drug product is adminis-
2 tered; and

3 “(II) will, in the aggregate, ac-
4 count for the total volume of drug
5 product compounded pursuant to the
6 non-patient-specific purchase order.

7 The compounding of a drug product may not be per-
8 formed under subparagraph (B) or (C) if
9 compounding under subparagraph (B) or (C), re-
10 spectively, is prohibited by the laws of the State in
11 which such compounding occurs or is prohibited by
12 the laws of any State in which the compounded
13 preparation is dispensed, sold, distributed, or
14 shipped.

15 “(3) UNITED STATES PHARMACOPOEIA CHAP-
16 TERS.—The drug product is compounded in compli-
17 ance with all United States Pharmacopoeia chapters
18 that are applicable to pharmaceutical compounding
19 (including the chapter on sterile preparations).

20 “(4) BULK DRUG SUBSTANCES.—The drug
21 product is compounded using bulk drug substances
22 (as defined in regulations of the Secretary published
23 at section 207.3(a)(4) of title 21 of the Code of Fed-
24 eral Regulations (or any successor regulations))—

25 “(A) that—

1 “(i) if an applicable monograph exists
2 under the United States Pharmacopoeia,
3 the National Formulary, or another com-
4 pendium or pharmacopeia recognized
5 under Federal or State law, each comply
6 with the monograph;

7 “(ii) if such a monograph does not
8 exist, each are drug substances that are
9 components of drugs approved by the Sec-
10 retary for human use; and

11 “(iii) if such a monograph does not
12 exist and the drug substance is not a com-
13 ponent of a drug so approved, each appear
14 on a list published by the Secretary
15 (through regulations issued under sub-
16 section (c));

17 “(B) that are each manufactured by an es-
18 tablishment that is registered under section 510
19 (including a foreign establishment that is reg-
20 istered under section 510(i)); and

21 “(C) that are each accompanied by a valid
22 certificate of analysis.

23 “(5) INGREDIENTS (OTHER THAN BULK DRUG
24 SUBSTANCES).—The drug product is compounded
25 using ingredients (other than bulk drug substances)

1 that comply with the standards of an applicable
2 United States Pharmacopoeia or National For-
3 mulary monograph.

4 “(6) DRUG PRODUCTS WITHDRAWN OR RE-
5 MOVED BECAUSE UNSAFE OR NOT EFFECTIVE.—The
6 drug product does not appear on a list published by
7 the Secretary (through regulations issued under sub-
8 section (c)) of drug products that have been with-
9 drawn or removed from the market because such
10 drug products or components of such drug products
11 have been found to be unsafe or not effective.

12 “(7) ESSENTIALLY A COPY OF A COMMER-
13 Cially AVAILABLE DRUG PRODUCT.—The licensed
14 pharmacists or licensed physician does not com-
15 pound any drug product that is essentially a copy of
16 a commercially available drug product.

17 “(8) DRUG PRODUCTS PRESENTING DEMON-
18 STRABLE DIFFICULTIES FOR COMPOUNDING.—The
19 drug product is not a drug product identified in a
20 list published by the Secretary (through regulations
21 issued under subsection (c)) as a drug product that
22 presents demonstrable difficulties for compounding
23 that demonstrate an adverse effect on the safety or
24 effectiveness of that drug product when administered
25 to or used by a patient.

1 “(9) VOLUME LIMITATION.—**[to be supplied]**

2 “(b) NOTIFICATION SYSTEM.—

3 “(1) DEVELOPMENT AND IMPLEMENTATION.—

4 The Secretary shall develop and implement a system
5 for receiving and reviewing submissions from State
6 boards of pharmacy—

7 “(A) describing actions taken against
8 compounding pharmacies; or

9 “(B) expressing concerns that a
10 compounding pharmacy may be acting as a
11 manufacturer of drug products in violation of
12 law.

13 “(2) CONTENT OF SUBMISSIONS FROM STATE
14 BOARDS OF PHARMACY.—An action referred to in
15 paragraph (1)(A) is, with respect to a pharmacy
16 that compounds drug products, any of the following:

17 “(A) The issuance of a warning letter, or
18 the imposition of sanctions or penalties, by a
19 State for violations of a State’s pharmacy regu-
20 lations pertaining to compounding.

21 “(B) The suspension or revocation of a
22 State-issued pharmacy license or registration.

23 “(C) The recall of compounded drug prod-
24 ucts due to concerns relating to the quality or
25 purity of such products.

1 “(3) CONSULTATION.—The Secretary shall de-
2 velop the system under paragraph (1) in consulta-
3 tion with the National Association of Boards of
4 Pharmacy.

5 “(4) REVIEW AND INSPECTION OF PHAR-
6 MACIES.—

7 “(A) REVIEW AND DETERMINATION BY
8 SECRETARY.—The Secretary shall—

9 “(i) review each submission received
10 under paragraph (1) and such other infor-
11 mation as the Secretary determines nec-
12 essary (including information collected
13 through an inspection or maintained in the
14 Adverse Event Reporting System data-
15 base); and

16 “(ii) make a determination as to
17 whether the pharmacy involved is in viola-
18 tion of one or more requirements of this
19 section.

20 “(B) REQUIRED INSPECTIONS.—

21 “(i) IN GENERAL.—Not later than 60
22 days after receiving a submission under
23 paragraph (1) regarding a pharmacy, the
24 Secretary shall—

1 “(I) assess whether there is evi-
2 dence suggesting that the pharmacy is
3 in violation of one of more require-
4 ments of this section; and

5 “(II) if the Secretary has reason
6 to believe that the pharmacy is in vio-
7 lation of one or more requirements of
8 this section, conduct an inspection of
9 the pharmacy to the extent necessary
10 for making a final determination
11 under such subparagraph (A)(ii).

12 “(ii) COORDINATION.—As the Sec-
13 retary deems appropriate, an inspection re-
14 quired by clause (i) may be conducted in
15 coordination with the relevant State board
16 or boards of pharmacy.

17 “(C) INSPECTION AUTHORITY.—The Sec-
18 retary may inspect a pharmacy—

19 “(i) to the extent necessary to deter-
20 mine whether the pharmacy is in violation
21 of one or more requirements of this section
22 if the Secretary has reason to believe the
23 pharmacy is in violation of such require-
24 ments; and

1 “(ii) to the extent necessary to deter-
2 mine whether the pharmacy has exceeded
3 the scope of the exemption under section
4 704(a)(2)(A) if the Secretary has reason to
5 believe that the pharmacy has exceeded
6 such scope.

7 “(5) NOTIFYING STATE BOARDS OF PHAR-
8 MACY.—The system under paragraph (1) shall be
9 designed to immediately notify State boards of phar-
10 macy when—

11 “(A) the Secretary receives a submission
12 under paragraph (1); or

13 “(B) the Secretary makes a determination
14 under paragraph (4)(A)(ii) that a pharmacy is
15 in violation of one or more requirements of this
16 section.

17 “(6) TIMING.—Not later than one year after
18 the date of enactment of the Compounding Clarity
19 Act of 2013, the Secretary shall begin implementa-
20 tion of the system under paragraph (1).

21 “(c) REGULATIONS.—

22 “(1) IN GENERAL.—The Secretary shall issue
23 regulations to implement this section.

24 “(2) ADVISORY COMMITTEE ON
25 COMPOUNDING.—Before issuing regulations to im-

1 plement subsections (a)(4)(A)(iii), (a)(6), and (a)(8),
 2 the Secretary shall convene and consult an advisory
 3 committee on compounding unless the Secretary de-
 4 termines that the issuance of such regulations before
 5 consultation is necessary to protect the public
 6 health. The advisory committee shall include rep-
 7 resentatives from the National Association of Boards
 8 of Pharmacy, the United States Pharmacopoeia,
 9 pharmacy, physician, and consumer organizations,
 10 and other experts selected by the Secretary.

11 “(3) UPDATING LISTS.—The Secretary shall
 12 update the regulations containing the lists under
 13 subsection (a)(4)(A)(iii), (a)(6), and (a)(8) regu-
 14 larly, but not less than once each year.

15 “(d) DEFINITIONS.—In this section:

16 “(1) The term ‘compounding’ does not include
 17 mixing, reconstituting, or other such acts that are
 18 performed in accordance with directions contained in
 19 approved labeling provided by the product’s manu-
 20 facturer and other manufacturer directions con-
 21 sistent with that labeling.

22 “(2) The term ‘essentially a copy of a commer-
 23 cially available drug product’ does not include—

24 “(A) a drug product in which there is a
 25 change, made for an identified individual pa-

1 tient, which produces for that patient a dif-
2 ference, as determined by the prescribing prac-
3 titioner, between the compounded drug and the
4 comparable commercially available drug prod-
5 uct; or

6 “(B) a drug product that appears on the
7 drug shortage list in effect under section 506E.

8 “(3) The term ‘licensed pharmacist’ includes
9 any individual that compounds drug products under
10 the supervision of a practitioner licensed to com-
11 pound drug products under State law.”.

12 **SEC. 3. PROHIBITION AGAINST INTENTIONAL FALSIFICA-**
13 **TION OF PRESCRIPTION ORDER FOR COM-**
14 **POUNDED DRUG PRODUCT.**

15 Section 301 of the Federal Food, Drug, and Cosmetic
16 Act (21 U.S.C. 331) is amended by inserting after para-
17 graph (bbb) the following:

18 “(ccc) The intentional falsification of a prescription
19 order for a drug product to be compounded under section
20 503A.”.

21 **SEC. 4. REVIEW OF ADVERSE EVENT REPORTING REGULA-**
22 **TIONS.**

23 The Secretary of Health and Human Services, acting
24 through the Commissioner of Food and Drugs, shall re-
25 view the regulations of the Food and Drug Administration

1 on adverse event reporting and determine whether any re-
 2 visions should be made with respect to adverse event re-
 3 porting by pharmacies engaged in compounding drug
 4 products.

5 **[SEC. 5. AMENDMENT TO SECTION 510.**

6 Section 510 of the Federal Food, Drug, and Cosmetic
 7 Act (21 U.S.C. 360) is amended—**]**

8 **[(1)** in subsection (a)(1), by inserting
 9 “compounding outside the scope of section 503A
 10 and” after “shall include”;**]**

11 **[(2)** in subsection (g)(1), strike “compound”
 12 and insert “compound outside the scope of section
 13 503A”; and**]**

14 (3) by adding at the end the following new sub-
 15 section:

16 “(q) COMPOUNDING OUTSIDE THE SCOPE OF SEC-
 17 TION 503A.—

18 “(1) FACILITY INSPECTION FEE.—**[to be sup-**
 19 **plied]**

20 “(2) STANDARDS.—**[to be supplied]**

21 “(3) OTHER.—**[to be supplied]**”.

Mr. PITTS. The Griffith draft includes targeted provisions that both clarify FDA's authority as it relates to Section 503 of the Food, Drug, and Cosmetics Act, while ensuring that traditional compounding remains within the purview of State boards of pharmacy.

I would like to welcome our witnesses.

And I will yield the balance of my time to Representative Griffith.

[The prepared statement of Mr. Pitts follows:]

PREPARED STATEMENT OF HON. JOSEPH R. PITTS

The subcommittee will come to order.

The Chair will recognize himself for an opening statement.

As we all know, in the summer and fall of 2012, a Massachusetts company, the New England Compounding Center (NECC), shipped over 17,000 vials of an injectable steroid solution from three contaminated lots to health care facilities across the country.

After receiving injections of NECC's contaminated steroid, over 50 people died from complications associated with fungal meningitis, and 700 others were stricken with meningitis or other persistent fungal infections.

The outbreak ranks as one of the worst public health crises associated with contaminated drugs in the history of the United States.

Shortly after the contamination came to light, the Committee began an investigation into the matter, requesting documents from the Food and Drug Administration (FDA) and the Massachusetts Department of Public Health; examining whether the outbreak could have prevented; and reviewing existing federal and state regulatory authority over compounding pharmacies acting as manufacturers.

Both this subcommittee and the Oversight and Investigations Subcommittee have held multiple hearings on the issues surrounding compounded drugs.

Today's witnesses are here to discuss three legislative proposals released since the outbreak, including a discussion draft authored by my colleague, Morgan Griffith.

The Griffith draft includes targeted provisions that both clarify FDA's authority as it relates to Section 503 of the Food, Drug and Cosmetics Act while ensuring that traditional compounding remains within the purview of state boards of pharmacy.

I would like to welcome our witnesses, and I would yield the remainder of my time to Rep. Griffith.

Mr. GRIFFITH. Thank you, Mr. Chairman. I appreciate that very much.

The fungal meningitis outbreak that was associated with the tainted sterile compounded drugs from the NECC is something that I have followed since the beginning. Obviously, you are always concerned when something affects anybody in the United States but particularly when it has the impact that it had in my district and in the areas immediately around my district, where we had 2 deaths, 50 confirmed cases, approximately 1,400 patients that were notified that they had gotten the tainted injects, creating great concern.

Now, I do acknowledge, and we have had hearings on it—and, Dr. Woodcock, you have been very good answering my questions, and I appreciate that—where we looked into it and found that the split in the circuits was caused by the issue on the advertising portions of the original bill. And as we previously discussed, it is a shame that this issue wasn't taken up sometime ago, but it wasn't. And we are here now, and we are going to try to clarify the law to make sure that we don't have this problem again. And I appreciate the fact that you are going to help us work on that.

You know, we have been following this. And what we want to do is make sure that we do, as the chairman said, protect public

health and ensure that small businesses, like the 130 legitimate community pharmacists that are located in my area, are not subject to unnecessary and burdensome Federal regulations. I also recognize the importance, as a former State legislator, that we continue to have the States be primary over the true local compounding pharmacies.

We have before us a draft. We are still working on it. We want to clarify the FDA's authority in this realm, particularly in regard to compounders who try to pretend that they are not manufacturers. And that is sometimes difficult, and I understand that, but we think that we have a bill that will help on that.

There are still questions that we are trying to get answered from stakeholders to complete the legislation. That is why in the draft you will see a couple of places where we have some blanks. I am proud to be trying to work out those differences with my colleagues across the aisle, Congressman Green and Congresswoman DeGette, to see if we can reach a bipartisan consensus and something that works to protect the health of Americans and protect the interests of small compounding pharmacies, which provide a great service to our public.

My goal has always been to draw a clear line on defining what a traditional compounding pharmacy is, and that should be regulated by the States, and what a manufacturer, a drug manufacturer is, which properly should be regulated by the FDA.

I look forward to today's hearing and from hearing from all of our witnesses as we continue this process to clarify FDA's authority when it comes to compounding pharmacies.

And I thank you, Mr. Chairman, for this opportunity and yield back my time.

Mr. PITTS. The chair thanks the gentleman and now recognizes the ranking member of the full committee, Mr. Waxman, for 5 minutes for an opening statement.

OPENING STATEMENT OF HON. HENRY A. WAXMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA

Mr. WAXMAN. Thank you, Mr. Chairman.

It has been 10 months since we saw the tragic fungal meningitis outbreak caused by the New England Compounding Center in Massachusetts. More than 60 people have died, over 740 people were sickened, and more than 13,000 others in 20 States are still waiting to see whether they will get meningitis. This is the largest outbreak of healthcare-associated infections in U.S. history and one of the Nation's worst public health disasters in recent memory.

We have learned a lot through our investigation, especially that FDA's authorities over compounding pharmacies are broken and inadequate. And I am glad we have finally begun the process of repairing them.

FDA has repeatedly testified that the agency desperately needs new authority to protect the public from another contamination incident. The agency has described how circuit court decisions have forced FDA to cobble together a piecemeal approach to regulating compounding pharmacies that are different in some parts of the country than in others. This has created loopholes that companies,

like the New England Compounding Center, have been able to exploit.

FDA has also described the fact that the pharmacy compounding industry has changed dramatically since 1997, when Congress last legislated. Hospitals have grown dependent on so-called outsourcers, which are very large compounding pharmacies that mix batches of customized drugs for a particular hospital.

FDA says it is not enough to simply fix the defect in the current statute. We need a new paradigm to handle this new state of affairs. The reason we need a new paradigm is that the new class of outsourcers does not fit neatly within the binary structure that exists in the current statute. They are neither traditional compounders nor drug manufacturers, so we need to tailor FDA's authorities to fit the reality that the agency faces.

But we also need to ensure that we properly circumscribe what these outsourcers can make so that they cannot become an avenue for undercutting FDA's gold-standard drug approval process. FDA needs strong records-inspection authority to be able to determine whether a compounding pharmacy is performing only a traditional compounding or has crossed the line into becoming an outsourcer or even a drug manufacturer.

In addition, these nontraditional compounders or outsourcers need to register with the FDA and tell FDA what drugs they are producing. They should be required to follow good manufacturing practices as set by the FDA and label their products as compounded so that healthcare providers and patients know that the products are not FDA-approved drugs.

As illustrated by the recent tragedy, these entities should also be required to promptly report adverse events to FDA so that FDA and the States can work together to identify dangerous compounded drugs and prevent them from reaching consumers.

In order for FDA to be successful at carrying out these new authorities, we need to ensure that FDA has a steady stream of resources. We will not have accomplished much if we enact a new statutory scheme but deny the FDA the dollars it needs to use its new authorities.

We have learned that there is a gaping hole in our drug safety laws. American families expect us to work together to develop an effective legislative response, and we need to do this as quickly as possible. We know that, otherwise, it will not be if another dangerous catastrophe occurs with compounded medicines, but when.

Thank you, Mr. Chairman. I yield back the balance of—unless any of my colleagues on the Democratic side would like the minute?

OK. I yield back the time.

Mr. PITTS. The chair thanks the gentleman and recognizes the vice chairman of the committee, Dr. Burgess, for 5 minutes for an opening statement.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. Thank you, Mr. Chairman.

You and the ranking member have said it very well. This is a continuation in this committee's examination of the meningitis out-

break that was caused by contaminated methylprednisolone acetate prepared in a preservative-free fashion that killed 53 Americans and harmed over 700, many of whom will suffer for the remainder of their lives with significant medical complications.

So 53 Americans are no longer here because the Food and Drug Administration refused to use their statutory authority to enforce existing regulations. I am willing to update the authority that the FDA already has. I don't know that I am willing to vest the FDA with new authority.

Besides refusing to use their existing statutory authority, the Food and Drug Administration is stalling the process to clarify existing regulations. We have been meeting for weeks now, both this subcommittee and the Oversight and Investigations Subcommittee, trying to determine how best to clarify existing regulations.

The Food and Drug Administration refuses to give an inch. They say they want clarity. Well, when we ask what kind of clarity, there is no answer. When we suggest a volume limitation by which to define a manufacturer, they say it is not workable. When we suggest a time period to determine whether an entity is a manufacturer, we get back, "It is not workable."

So my ask to the FDA is: Stop telling us it is not workable, and start helping us with a practical solution. If you are holding out for a power grab for a vast, new, unfunded authority, I am not going to help you get there.

So far, the only thing I have heard from the Food and Drug Administration are complaints about sequestration. I get it. They complain that user fees don't address their financial needs, especially under sequestration. I really get it. But to have the Food and Drug Administration come to Congress, seeking completely new user fees and authorizations to inspect facilities, when existing regulations clearly give the authority to inspect anyone who is a manufacturer, I have to tell you, I just don't get it.

The fact that the Food and Drug Administration has continued to inspect facilities—they have closed facilities. How are they inspecting these facilities if they have no authority to do so?

Representative Griffith's bill represents the best effort to date to address some of the FDA concerns while adhering to the spirit of the law. And I am comfortable supporting that bill. But, honestly, all the laws in the world are not going to save a single patient if there is no one enforcing the law.

We read the chain of emails from two administrations of the Food and Drug Administration. It was painful to read those emails. They would come right up to the edge, right up to the point where they might close someone down, and then say, well, we can't send another warning letter because we have already sent too many, so we don't know what to do. Well, I know what to do: Close the place down. It was the right answer, and it still is today.

Who at the Food and Drug Administration has been fired over this incident? Again, 53 Americans died, 700 are living with a disability. Who has been fired in this exercise?

So I would say enough is enough. Let's put pen to paper and make sure the bad actors are not able to hide from clear enforcement authority, but let's make sure the enforcement authority is actually going to be enforced.

Mr. Chairman, I thank you for the time, and I yield back to you.

Mr. PITTS. The chair thanks the gentleman.

I would like to thank all of our witnesses for coming.

On our first panel today, we have Dr. Janet Woodcock, director of the Center for Drug Evaluation Research of the U.S. Food and Drug Administration.

Thank you very much for coming, Dr. Woodcock. You will have 5 minutes to summarize your testimony. Your written testimony will be entered into the record. So, at this time, you are recognized for 5 minutes for your opening statement.

STATEMENT OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION

Dr. WOODCOCK. Thank you.

Since the last hearing before this subcommittee, which was just 7 weeks ago, we have had another multi-State outbreak involving contaminated methylprednisolone acetate, preservative-free. Even with all the publicity and attention surrounding this problem, we are still seeing multiple contaminated compounded products on the market.

We really appreciate the committee's interest in exploring legislative options to try to help prevent future tragedies. And I would like to start with what I think are the common legislative goals I hope we all share.

Any legislation that is passed should provide clarity so that people know who is on first—FDA, the States, compounders, and healthcare providers all know their roles and responsibilities and obligations under the law.

We feel that there should be a legal framework that is a better fit for the industry that has now evolved and is well beyond compounding by a corner pharmacy for a single patient, by prescription, in response to a practitioner from a medical need. It has gone well beyond that. We have outsourcers who supply large amounts of sterile products to hospitals across the country.

Enforceability: We need legislation that we can implement on the ground, that we can actually make work, and is resourced to be successful.

We need to preserve the benefits of traditional compounding. We have always recognized these benefits, where there is a medical need not met by the products that are FDA-approved. And we need to preserve the ability of pharmacists to compound and physicians and other prescribers to order compounded products to meet those medical needs.

And, most importantly, we need better protection of the public by bringing the highest-risk practices under Federal oversight. This includes really focusing on prevention rather than reaction when outbreaks are occurring.

We want to work with you to achieve those goals. We believe that for the highest-risk compounding pharmacies we do need legislation that requires Federal registration so we know who they are and where they are, that holds them to Federal quality standards, which we call the GMPs, for production, that also requires the compounders to tell us when serious adverse events related to their

products are reported to them so that we can intervene before these problems get out of hand.

And we think for all pharmacy compounding, certain basic protections should be in place, including clear authority for us to inspect records so we can determine the cause of an outbreak or decide whether a compounder actually fits into the highest-risk category; restrictions on compounding complex products that even conventional drug manufacturers, who test their products, find difficult to produce safely; and a requirement to start with safe and high-quality ingredients when you are compounding.

And, finally, we feel that clear labels on compounded drugs to allow prescribers and patients to make informed choices are important.

We appreciate the leadership of Mr. Griffith, Mr. Markey, and the Senate HELP Committee in drafting legislation to try and tackle these issues. It is not easy. While the administration has not taken a position on any of these bills, I am happy to provide my views on the extent to which they address the goals that we have for any new compounding legislation.

The fungal meningitis outbreak has been a nightmare that continues for over 700 people sickened by these drugs and their families. And it is just the worst of a long series of outbreaks over the past 2 decades that include deaths, blindness, and hospitalizations.

And this continues. As we proceed with our inspections—we have had 61 and counting—of the industry, we continue to see a pattern of profoundly disturbing lapses in basic sterile practices that should be in place to assure the sterile drugs—the drugs that are injected in the blood, the spine, the eye, and so forth—are actually sterile.

So I reiterate my statement from the hearing you held 7 weeks ago. It is a matter of when this is going to occur, not whether it is going to occur. We owe it to the public and the victims of this incident and the numerous other outbreaks over the years to enact legislation that provides better protection in the future.

I look forward to answering your questions.

[The prepared statement of Dr. Woodcock follows:]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

**STATEMENT
OF
JANET WOODCOCK, M.D.
DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON ENERGY AND COMMERCE
U.S. HOUSE OF REPRESENTATIVES
“REFORMING THE DRUG COMPOUNDING REGULATORY FRAMEWORK”**

July 16, 2013

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss important issues related to pharmacy compounding.

We are at a critical point where we must work together to improve the safety of drugs produced by compounding pharmacies. As the compounding industry has grown and changed, we have seen too many injuries and deaths over many years caused by unsafe practices. Dr. Margaret Hamburg, Commissioner of Food and Drugs, testified in front of the Oversight and Investigations Subcommittee on November 14, 2012, and April 16, 2013, regarding the tragic fungal meningitis outbreak associated with compounded methylprednisolone acetate (MPA), a steroid injectable product distributed by the New England Compounding Center (NECC). I testified in front of this Subcommittee on May 23, 2013, and provided additional details on the framework FDA has developed that could serve as the basis for the development of a risk-based program to protect the public health.

As both Dr. Hamburg and I testified, NECC was not an isolated incident. Indeed, over the past 20 years, we have seen multiple situations where compounded products have caused deaths and serious injuries. Also, we both testified that it is a matter of when, not if, another contamination incident will occur with compounded products. And since the NECC outbreak, we have identified contaminated products at other pharmacies and widespread sterile production issues

that have led to recalls and shutdowns of compounding operations. In one recent incident, the presence of floating particles, later identified to be a fungus, was reported in five bags of magnesium sulfate intravenous solution, resulting in a nationwide recall of all sterile drugs (over 100 products) produced by Med Prep Consulting, Inc., a state-licensed facility in Tinton Falls, New Jersey. Med Prep manufactured and repackaged sterile drug products for hospitals and health care facilities, including products intended to be injected into the vascular system of patients. After learning of the contaminated product, FDA conducted a for-cause inspection of Med Prep and issued an FDA Form 483,¹ which noted serious deficiencies in Med Prep's sterile processing. Thereafter, the Department of Justice, on behalf of FDA, filed a complaint for permanent injunction against Med Prep Consulting, Inc. in the U.S. District Court for New Jersey. The parties have signed a Consent Decree of Permanent Injunction, which was entered by the Court on June 27, 2013. The consent decree enjoins Med Prep and its president and owner from manufacturing, holding, and distributing drug products until they comply with certain requirements of the Federal Food, Drug, and Cosmetic Act and all applicable regulations.

In another recent recall, all sterile drug products (approximately 60 products) from a second pharmacy were recalled as a result of reports that five patients were diagnosed with serious eye infections associated with the use of repackaged Avastin. The firm has stopped all sterile compounding.

And just since I last testified six weeks ago, FDA has received reports of adverse events, including skin and soft tissue abscesses associated with Main Street Family Pharmacy's (Main Street) preservative-free methylprednisolone acetate for injection. FDA began to investigate immediately after receiving these reports, and, to date, we are not aware of any cases of

¹ An FDA Form 483 is issued when investigators observe any significant objectionable conditions. It does not constitute a final Agency determination of whether any condition is in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act) or any of our relevant regulations, but the observations often serve as evidence of a violation of the FD&C Act and its implementing regulations.

meningitis associated with Main Street's products. However, Main Street, a Newbern, Tennessee, pharmacy licensed by the state of Tennessee, shipped methylprednisolone acetate to 17 states and other sterile products to at least 34 states. On May 28, 2013, Main Street announced a voluntary nationwide recall of all sterile products compounded by the pharmacy. The compounded products that are subject to the recall are those products with a use-by date on or before November 20, 2013. FDA issued an FDA Form 483 to Main Street on June 11, 2013. The 483 listed observations, including the presence of spiders in the clean room, failure to use a sporicidal cleaning agent, failure to clean equipment to prevent contamination, poor personnel aseptic practices, failure to review batch specification failures, failure to perform endotoxin and sterility testing, failure to obtain data to support expiration dates, failure to perform routine calibration on equipment, failure to retain samples of injectable drugs, inadequate record keeping, and failure to separate expired products from in-date products. The investigation into this matter is ongoing.

These are just some of the cases we've seen since the fungal meningitis outbreak. To date, since September 26, 2012, FDA is aware of 17 firms that have conducted recalls—12 firms have conducted recalls overseen by FDA² and five firms have conducted recalls overseen by the state in which the firms are located. In addition, since September 26, 2012, we are aware of 19 firms that ceased sterile operations, in some cases voluntarily, and in other cases due to partial or full shutdowns imposed by state licensing authorities. FDA has issued two Warning Letters to date. However, we believe that presently, there are many other firms operating as compounding pharmacies, producing what should be sterile products and shipping them across state lines in

² While in most instances firms eventually agree to voluntarily recall drugs that FDA believes pose a risk, FDA lacks the authority to compel such recalls, and critical time can be lost in negotiations between FDA and a firm, leaving the public exposed to potentially serious health risks. The Agency has mandatory recall authority for medical devices, infant formula, and many other foods, but not for drugs.

advance of or without a prescription. These pharmacies are licensed by the states and generally are not registered with FDA. We may not even become aware of a firm's existence until it has already produced drugs that have caused patients harm.

Notably, even in light of recent events, and even though we are often working with the state inspectors, our investigators' efforts are being delayed because they are denied full access to records at some of the facilities they are inspecting. Just during the recent inspections, several pharmacies delayed or initially refused FDA access to records, and FDA had to seek administrative warrants in two cases. And although we have been able to eventually conduct the inspections and collect the records that we have sought, our ability to take effective regulatory action to obtain lasting corrective action with regard to substandard sterility practices remains to be seen.

The history of pharmacy compounding shows that there is a need for appropriate and effective oversight of this evolving industry. The industry and the health care system have evolved and outgrown the law, and FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients must evolve as well.

Limitations and ambiguities in the law have led to legal challenges to FDA's authority to inspect pharmacies and take appropriate enforcement actions.

FDA's Recent Efforts

Using a risk-based model, we identified 29 firms for priority inspections focused on their sterile processing practices. During these 29 inspections, in two instances, FDA identified secondary firms associated with the priority inspections, for a total of 31 firms. We have taken investigators who would normally be doing inspections of conventional drug manufacturers and assigned them to conduct inspections of those pharmacies whose history suggests a greater risk

of potential quality issues with their compounded products. We have coordinated our inspections with state officials, who have accompanied our investigators in most cases. At the same time, we have also continued to conduct for-cause inspections, often at the request of our state counterparts who invited us to accompany them on the inspections. Since the fall, FDA has completed 31 for-cause inspections in addition to the 31 described above, as of June 30, 2013.

When we identified problems during any of these inspections, at the close of the inspection, we issued an FDA Form 483 listing our inspection observations. We have issued an FDA-483 at the close of 52 of the 62 inspections we have conducted since last fall. As described above, we have seen serious issues, including practices that create a risk of contamination and other quality concerns. While firms have voluntarily recalled products in some of these cases, recalls are a temporary fix designed to get product off the market immediately. We need to do everything we can to clarify and strengthen FDA's authority in this area.

As we have noted in the past, our ability to take action against inappropriate compounding practices has been hampered by ambiguities regarding FDA's enforcement authority, legal challenges, and adverse court decisions interpreting that authority. For example, hospitals have come to rely on compounding pharmacies that function as "outsourcers" producing sterile drugs previously made by hospital in-house pharmacies. If FDA were to bring charges against a pharmacy, alleging that it is manufacturing a "new drug" that cannot be marketed without an approved application, the pharmacy would have to either obtain individual patient-specific prescriptions for all of its products or stop distributing the products until it obtains for them approved New Drug Applications (NDA),³ something most outsourcers are unlikely to do. Specifically, a new drug application must include proof that the drug is safe and effective and be

³ Compounded drugs generally could not satisfy the requirements of an abbreviated NDA, which include evidence that the drug is the same as the reference listed drug in dosage form, strength, route of administration, quality, performance characteristics, and intended use.

accompanied by an application fee set by the reauthorization of the Prescription Drug User Fee Act (PDUFA) last year. FDA drug approvals are manufacturer-specific, product-specific, and include requirements relating to the product. Many outsourcers compound hundreds of products, each of which would require a separate application.

Outsourcers can provide valuable services if they compound drugs under certain conditions, including adhering to applicable Federal quality standards. For example, many hospitals rely on outsourcers to produce specialized dilutions of FDA-approved products to be used in anesthesia during surgery. However, outsourcers are unlikely to submit an NDA for each of the many specialized products hospitals request. While the health care system has grown to rely on obtaining these products from outsourcers, if they are produced under substandard sterile conditions, the risks to patients can outweigh any perceived benefits. These outsourcers are not traditional pharmacy compounders as they are compounding products without patient-specific prescriptions that are administered to sometimes thousands of patients nationwide. FDA's authorities should be appropriately tailored to effectively oversee these compounding activities.

FDA's Legal Authority over Compounded Drugs

In the Commissioner's appearances before the Committee on Energy and Commerce in November 2012 and April 2013, and my appearance in May 2013, we presented a framework that could serve as a basis for the development of a risk-based program to better protect the public health, improve accountability, and provide more appropriate and stronger tools for overseeing this evolving industry. Since November, we have met with over 50 stakeholder groups, including pharmacy, medical, hospital, payer, and consumer groups, and state regulators, to help further our understanding and inform our framework. I will now provide background on FDA's current legal authority over compounded drugs, then review that framework, and suggest

specific actions that Congress can take to help us better do our job and prevent future tragedies like this one.

FDA believes that pharmacists engaging in traditional compounding provide a valuable medical service that is an important component of our health care system. However, by the early 1990s, some pharmacies had begun producing drugs beyond what had historically been done within traditional compounding.

After receiving reports of adverse events associated with compounded medications, FDA became concerned about the lack of a policy statement on what constituted appropriate pharmacy compounding. In March 1992, the Agency issued a Compliance Policy Guide (CPG), section 7132.16 (later renumbered as 460.200) to delineate FDA's enforcement policy on pharmacy compounding. It described certain factors that the Agency would consider in its regulatory approach to pharmacies that were producing drugs.

The compounding industry objected to this approach and several bills were introduced, some with significant support, to limit the Agency's oversight of compounding.⁴ In November 1997, S. 830, the Food and Drug Administration Modernization Act of 1997 (FDAMA), was signed into law as Public Law 105-115.⁵ FDAMA added Section 503A to the FD&C Act, to address FDA's authority over compounded drugs.⁶ Section 503A exempts compounded drugs from three critical provisions of the FD&C Act: the premarket approval requirement for "new drugs"; the requirement that a drug be made in compliance with current Good Manufacturing

⁴ H.R. 5256, Pharmacy Compounding Preservation Act of 1994, introduced Oct. 7, 1994, 1 co-sponsor; H.R. 598, Pharmacy Compounding Preservation Act of 1994, introduced Jan. 20, 1995, 141 co-sponsors; H.R. 3199, Drug and Biological Products Reform Act of 1996, introduced March 29, 1996, 205 co-sponsors; H.R. 1060, Pharmacy Compounding Act, introduced March 13, 1997, 152 co-sponsors; H.R. 1411, Drug and Biological Products Modernization Act of 1997, introduced April 23, 1997, 16 co-sponsors

⁵ Public Law 105-115, FDAMA, 111 Stat. 2296 (Nov. 21, 1997), available at <http://www.gpo.gov/fdsys/pkg/PLAW-105publ115/pdf/PLAW-105publ115.pdf>

⁶ Id.

Practice (cGMP) standards; and the requirement that the drug bear adequate directions for use, provided certain conditions are met. These provisions were the subject of subsequent court challenges, which have produced conflicting case law and amplified the perceived limitations and ambiguity associated with FDA's enforcement authority over compounding pharmacies. In 2002, immediately after a Supreme Court ruling that invalidated the advertising provisions of Section 503A, FDA issued a revised CPG on compounding human drugs. Several additional legal challenges and court decisions then followed. More recently, FDA made significant progress toward issuing another CPG. In fact, FDA was on track to publish a revised draft CPG in the fall of 2012, but the fungal meningitis outbreak intervened and we are now re-evaluating the draft. It is important to note, however, that a CPG is not binding on industry, and updating the CPG would not alleviate all issues with Section 503A.

A look at FDA's attempts to address compounding over the last 20 years shows numerous approaches that were derailed by constant challenges to the law. As a result, presently, it is unclear where in the country Section 503A is in effect, and Section 503A itself includes several provisions that have impeded FDA's ability to effectively regulate pharmacy compounding practices. Apart from Section 503A, there are additional provisions in the statute that have impeded effective pharmacy compounding regulation. For example, the FD&C Act exempts certain compounding pharmacies from registration and the obligation to permit access to records during an inspection. As a result, FDA has limited knowledge of pharmacy compounders and compounding practices and limited ability to oversee their activities.

Looking Ahead

The Administration is committed to working with Congress to address the threat to public health from limitations in authorities for effective oversight of certain compounding practices. To that

end, FDA has developed a framework that could serve as the basis for the development of a risk-based program to protect the public health.

Risk-based Framework

Recognizing the history of compounding practice, FDA supports the long-standing policy that all compounding should be performed in a licensed pharmacy by a licensed pharmacist (or a licensed physician), and that there must be a medical need for the compounded drug.

Further, we believe there should be a distinction between two categories of compounding: traditional and non-traditional. Traditional compounding would include the combining, mixing, or altering of ingredients to create a customized medication for an individual patient with an individualized medical need for the compounded product, in response to a valid patient-specific prescription or order from a licensed practitioner documenting such medical need. Traditional compounding, while posing some risk, plays an important role in the health care system and should remain the subject of state regulation of the practice of pharmacy.

Non-traditional compounding would include certain types of compounding for which there is a medical need, but that pose higher risks. FDA proposes working with Congress to define non-traditional compounding based on factors that make the product higher risk such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the state in which it was produced. Non-traditional compounding would be subject to Federal standards adequate to ensure that the compounding could be performed without putting patients at undue risk, and FDA would inspect against and enforce these Federal standards. Such a definition focuses on the highest risk activities and offers a uniform degree of protection across all 50 states, for highest-risk compounding activities.

Non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight. Sterile products produced in advance of or without a prescription and shipped interstate should be subject to the highest level of controls, established by FDA and appropriate to the activity, similar to cGMP standards applicable to conventional drug manufacturers.

In addition, FDA believes that with noted exceptions, certain products are not appropriate for compounding under any circumstances. These products would include: 1) what are essentially copies of FDA-approved drugs, absent a shortage justification based on the drug appearing on FDA's shortage list; and 2) complex dosage forms such as extended-release products; transdermal patches; liposomal products; most biologics; and other products as designated by FDA. Producing complex dosage forms would require an approved application and compliance with cGMP standards, along with other requirements applicable to manufactured drug products.

FDA believes that there are other authorities that would be important to support this new regulatory paradigm. For example, FDA should have clear ability to collect and test samples of compounded drugs and to examine and collect records in a compounding pharmacy, just as the Agency does when inspecting other manufacturers. FDA should also have clear ability to examine records, such as records of prescriptions received, products shipped, volume of operations, and operational records, such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding, to respond to public health threats, and to enforce Federal standards.

FDA also believes that an accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with state regulators. In addition, FDA looks forward to working with Congress on potential improvements that may include label statements and adverse event reporting that have proven useful in other areas. A user-fee-funded regulatory program may be appropriate to support the inspections and other oversight activities outlined in this framework. We look forward to working with Congress to explore the appropriate funding mechanisms to support this work, which could include registration or other fees, as Congress has authorized and FDA has successfully implemented in other settings.

CONCLUSION

Given our experiences over the past 20 years and the recent fungal meningitis outbreak, we must do everything we can to clarify and strengthen FDA's authority in this area. I am happy to answer any questions you may have.

Mr. PITTS. The chair thanks the gentlelady.

And I will begin the questioning and recognize myself for 5 minutes for that purpose.

Dr. Woodcock, isn't it true that, assuming the circuit split ambiguity is resolved, FDA now has the authority to regulate nontraditional compounders as manufacturers?

Dr. WOODCOCK. Yes, that is true.

Mr. PITTS. Doesn't that mean that FDA could already require that such compounders pay user fees and submit applications to show that they can produce drugs under GMP conditions?

Dr. WOODCOCK. That is a possible outcome. We would have to find out who they are, because they don't register, and where they operate. And it is possible even if we close one entity down, another could quickly grow up.

There is no real preventive structure here; this is a reactive structure that would rely upon us finding these folks and taking action. And it isn't clear in the judiciary if we would prevail because of still-remaining ambiguities in the law.

Mr. PITTS. In your testimony, you note that there is need for appropriate and effective oversight of the pharmacy compounding industry. According to the FDA, this industry and the healthcare industry have evolved and outgrown the law.

How do you recommend we draft this legislation to ensure that this industry does not outgrow this legislation?

Dr. WOODCOCK. Well, I think one of the keys—and I recognize it is very hard—is making that distinction between traditional pharmacy compounding, which was for a single patient, medical need, prescription for that compounded product, and the kind of practices that are going on now. And those practices involve making large batches often, small to large batches, and of course shipping them many places, often without a prescription.

Mr. PITTS. Now, are large-scale compounders, compounding manufacturers we would call them, more similar to pharmacies or manufacturers? What qualities do they share with manufacturers?

Dr. WOODCOCK. They share with manufacturers the fact that they are manipulating drug products and making them in batches, large to small batches, and shipping them to various places.

They share with pharmacies that many of the practices that they are doing used to be done in the hospital pharmacy, and the hospital pharmacies have outsourced much of these operations because they don't have the appropriate facilities. But, frankly, no one is looking to see if these new outsourcers have the appropriate facilities and practices.

Mr. PITTS. Considering that they are more similar in function to manufacturers, should they be regulated within the manufacturing framework?

Dr. WOODCOCK. They are similar but not identical. Most of them make large numbers of different products in much smaller amounts than a pharmaceutical manufacturer would make. Many of them are starting from FDA-approved products and putting them in syringes or little IV bags and all sorts of things for the particular doctor or practice or hospital and what their needs are, all right?

So if you wish to have NDAs and the entire panoply of the FDA review process, what we do for regular pharmaceutical manufactur-

ers, this industry could probably not exist, all right? So that is a choice that you have to make. Do you create a new framework that encompasses this, or do you want to stick to the current binary structure that we have?

Mr. PITTS. Would it be better to regulate large-scale compounders under the manufacturing standards rather than establishing a new category?

Dr. WOODCOCK. We believe that the main issue with these large-scale, especially sterile, compounders is that they are not following what we call aseptic processing practices that are appropriate, which are part of our good manufacturing processes, OK, and practices.

And we feel that if that was required, to use appropriate sterile processing and certain other aspects of the good manufacturing practices, that they could make quality products that would be safe.

Mr. PITTS. Under the proposed Senate framework, FDA would be barred from requiring compounding manufacturers to submit NDAs and ANDAs pre-inspection and labeling requirements before these drugs reach patients.

Would any of these tools be available to FDA as it relates to compounding manufacturers, even if agency regulators identified high-risk compounding manufacturers where they, upon inspection, thought such tools were appropriate to utilize in order to protect public health?

Dr. WOODCOCK. Well, we need to have tools that prevent this industry in general from subverting the new drug review process and the generic drug review processes that were established by Congress a long time ago and have served us very well. So there have to be provisions that make a distinction between what constitutes manufacturing a new drug or a generic drug and these practices. And that is not easy or straightforward to do.

But we have proposed that for all compounding pharmacies that there be certain things that they would not be doing. They would not be making copies of FDA-approved drugs, for example. Why would you need a higher-risk product if there were approved drugs available?

We have also proposed that medical need might be a criterion. That is really the reason you use a compounded drug, is because there isn't an FDA-approved drug available for that medical need. And so that is the reason that compounding exists, to meet that need.

Mr. PITTS. Thank you. My time has expired.

The chair recognizes, filling in for Ranking Member Pallone, Mr. Green of Texas, for 5 minutes for questions.

Mr. GREEN. Thank you, Mr. Chairman.

Dr. Woodcock, thank you for continuing your willingness to advise the subcommittee on this subject. The question that has been at the forefront of our policymaking is how to establish a bright line between State and Federal jurisdiction between the traditional compounders and those operating closer to manufacturers. No approach is without its challenges, and certainly none are perfect.

I understand that a lot of the FDA answers are premised on the fact that you cannot know what you don't know before you know

it. However, under the assumption that you get the records inspection authority necessary to look at the records of the suspect entities, that there are other factors that Congress gives you to establish risk, such as sterility, interstate commerce, and the existence or not of a prescription.

With that in mind, how can we go about setting a production volume level threshold as a proxy for assessing risk? Other than the options that are on the table from the Markey, Griffith, and Senate drafts, how else can we go about targeting our regulations toward the highest-risk entities?

Dr. WOODCOCK. Well, one thing we don't want to do, in talking about volume or those types of things, is create a large loophole so that manufacturers can actually circumvent the entire legislation.

The problem with volume is that the traditional compounding volume unit is one. It is one compounded product that is made in response to one patient's medical need—

Mr. GREEN. Which is currently regulated under State law.

Dr. WOODCOCK. Yes. And that is the way it should be, we feel. That is a traditional pharmacy practice.

The risk of that is limited by many things. If you make one sterile product, one transfer, you have less personnel, you have less manipulations. Obviously, the exposure, if you make a lot, 17,000 or 7,000, then the risk is spread across many people. But the actual risk as you go from 1 to 10 to 100 increases, and so it is hard to make a bright line on—

Mr. GREEN. OK. There is other criteria other than volume. Length of time. I have seen 7 days, we have seen 10 days. Because if you are warehousing this product on a shelf, it can deteriorate and bacteria can grow, which is, I assume, what happened up in Massachusetts. So we are looking at, also, some kind of timeframe for the use of that drug; is that correct?

Dr. WOODCOCK. Timeframe could be a criterion that could be used. You know, we have put forth criteria—

Mr. GREEN. Well, we are looking at multiple criteria, I hope.

Dr. WOODCOCK. Certainly, the longer any sterile drug product is stored, or any drug product for that matter, the riskier it becomes.

And one of the reasons the hospitals gave the IG, when they did their survey, of why they outsourced the products is they say that compounded products have a longer beyond-use date. They might have up to 6 months. But, in our inspections, what we found is they didn't establish that by testing. They just maybe looked in a compendium or something and said, well, 6 months looks like a good beyond-use date. They had no data to back it up.

Mr. GREEN. OK.

Dr. Woodcock, the National Association of Boards of Pharmacy are testifying on our second panel, and they suggest a revision of the FDA's proposed statutory framework for traditional compounders. Their goal is to allow patients to access limited amounts of compounding products made by traditional compounders in advance of a prescription when they are in clinics, doctors' offices, or other healthcare settings. And I would use the example of a hospital, for example, made by from a compounder because of, you know, the volume.

Specifically, one of the limitations they suggest is to limit the total quantity provided to a healthcare provider to a 10-day patient supply. What are your views on that?

Dr. WOODCOCK. Well, my understanding is that 10 days would be the amount that that entity, healthcare entity or clinic, whatever, needed for 10 days. Right? And so, say they needed 50 vials; they used up 50 vials in 10 days. And then the clinic shifted to 100 providers. That would be 5,000, right?

So I don't know that that is a very good—and then you would make a batch of 5,000 and that would be OK. So I am not sure that is OK.

Mr. GREEN. Well, the other concern from your earlier testimony is that we want to make sure that that longevity, the efficiency of that compounding substance is actually 10 days instead of whatever you guess it is. Other pharmaceuticals have to show that their shelf life—

Dr. WOODCOCK. Yes. Under the GMPs, if we had Federal regulation of a sector, we would require that stability be demonstrated.

Mr. GREEN. Well, again, I am out of time, but I appreciate you working with both Congressman Griffith Congresswoman DeGette and I and our ranking members to see how we can get this right.

Thank you, Mr. Chairman.

Mr. PITTS. The chair thanks the gentleman and now recognizes the vice chairman, Dr. Burgess, for 5 minutes for questions.

Mr. BURGESS. I thank the chairman.

So, Dr. Woodcock, you know, we have these large outsourcers. And is that part of the problem, you don't know who they are?

Dr. WOODCOCK. We have large outsourcers; we don't know who they are. They are doing a variety of things, including making a lot of convenience dosage forms for hospitals and clinics. They are also compounding from bulk for shortages, making hyperalimentation and so forth—

Mr. BURGESS. Let me ask you a question about that then. Are they not already required to register with the Food and Drug Administration under Section 510 of the act?

Dr. WOODCOCK. Not according to them.

Mr. BURGESS. But according to you. I mean, you are the enforcer.

Dr. WOODCOCK. If we can find them and we can conclude that they are, you know, violating—that they are required to register. But, according to them, they are registered pharmacies in their—whatever State, doing pharmacy operations.

Mr. BURGESS. Those small pharmacies that compound as a result of receipt of a prescription, I mean, they are exempt under the law.

Dr. WOODCOCK. Yes.

Mr. BURGESS. And there is value in that. I mean, we all get it, that if a kid needs Tamiflu and there is no pediatric formulation available, someone needs to be able to crush up the tablet and mix it with the cherry favoring so that the kid gets it. We all want that.

But this is not that situation. These are companies that make a large volume, and they make it not on receipt of a prescription. They make it well in advance of anyone ordering it. So, for all the world, they look like a manufacturer to anyone else.

Dr. WOODCOCK. Well, I wish the distinction were that simple. However, as I just stated, if you have a pharmacy that is making

office stock and they are going to give that clinic 50 vials a week, all right, in response to a usual need, which is a practice in many States that is allowed, all right, and they have 100 customers, then they are going to be making a batch every week or perhaps every 2 weeks of 5,000 to 10,000 vials.

Mr. BURGESS. But—

Dr. WOODCOCK. And is that different? I mean, they are allowed under the State pharmacy laws to have anticipatory compounding.

Mr. BURGESS. So they would be regulated by the State boards of pharmacy, would they not?

Dr. WOODCOCK. Yes. They have to have a pharmacy license, uh-huh.

Mr. BURGESS. So they are licensed and regulated. Now, when they engage in interstate sales, that seems like it would come under your jurisdiction, would it not?

Dr. WOODCOCK. My understanding is there are reciprocal licensing agreements amongst the various boards of pharmacy in all the different States.

Mr. BURGESS. I just have to tell you, it doesn't sound like a gap in the statute, it sounds like an enforcement issue. And from everything that we received on the events leading up to the New England Compounding Center disaster, I mean, there were people within your agency over and over again that said, "Well, we can't just send them another warning letter. We have to actually do something." And then they would get to the point of doing something, and no one would do it.

Let me just ask you again. I mean, I assume there has been some sort of internal look at the breakdowns in the system as they existed in the Food and Drug Administration; am I correct?

Dr. WOODCOCK. Yes.

Mr. BURGESS. And have there been disciplinary actions taken against any individuals?

Dr. WOODCOCK. Well, this is more a collective failure than an individual failure. We are now using our authorities very aggressively—

Mr. BURGESS. OK, let me stop you for a second. A collective failure, and we want to give you new authority? I mean, honestly, do you see the problem with that logic?

Dr. WOODCOCK. I understand your problem. However, we are right now being very aggressive in using our existing authority.

Mr. BURGESS. Correct. And you are using that existing authority, and you are using it to the end that you are inspecting people, and you have closed some people down, have you not? I mean, before Main Street Pharmacy, you had closed other entities down. When either you or Dr. Hamburg came here earlier this year, you probably told us about some people you had closed down.

Dr. WOODCOCK. We have taken actions. You know, basically, the State boards of pharmacy have closed a number of entities down. We have taken other judicial actions. It remains to be seen if these are contested.

Mr. BURGESS. Right. But the Food and Drug Administration has—I mean, they have shown up with their official FDA jackets and seized records and seized product and closed facilities down, did you not?

Dr. WOODCOCK. We have done 61 inspections, and we found many serious violations of sterile practices and many products that are posing risk to the public.

Mr. BURGESS. So this is what I just don't get. You have the authority, since October of 2012 or whenever it was that we decided to do this, but you didn't have it the year before. And nothing has changed in statute over that time. So you had the authority in 2006, 2007, 2008, 2009, did you not?

Dr. WOODCOCK. We had the authority we have now. We feel—

Mr. BURGESS. Yes.

Dr. WOODCOCK [continuing]. Our authority is limited. But we can do the things that you say, and we are doing those.

Mr. BURGESS. It doesn't look limited to somebody looking from the outside. It looks like you are exercising your authority and it is working.

Dr. WOODCOCK. Well, for example, we have received reports of contaminated products and injuries of people from pharmacies we have never heard of. Now, it is hard for me to imagine—you know, I am somebody who is an executive. OK, manage things. How am I going to find these and anticipate that they are going to cause problems and shut them down if I have never even heard of them?

Mr. BURGESS. Well, Mr. Chairman, I know my time has expired.

I may ask you this question in writing. I would just really like to know how you expect to do that under the new authority that the Senate bill is proposing or that Mr. Markey has proposed.

But I will yield back my time, Chairman.

Mr. PITTS. The chair thanks the gentleman and now recognizes the ranking member of the full committee, Mr. Waxman, for 5 minutes for questions.

Mr. WAXMAN. Thank you, Mr. Chairman.

There was a provision, Dr. Woodcock, in the bill that Mr. Griffith introduced that I want to ask you about. It says that so long as a company holds a valid State pharmacy license and receives assurances from the healthcare providers to whom they are sending compounded drugs that the providers will send back prescriptions within 7 days after administering the compounded drug, that the company is considered to be doing traditional pharmacy compounding within the scope of State law.

In other words, regardless of the quantity of compounded medicines a company is making and whether the company is shipping those medicines all over the country, so long as that company receives prescriptions from their customers within 7 days after the medicines are actually given to the patient—who knows when that will be—there will be no Federal oversight of that company.

This seems like a particularly dangerous structure to me. It would allow a company like NECC, which caused the fungal meningitis outbreak, to operate freely without FDA oversight so long as it made a relatively minor change in its business practice: keeping copies of prescriptions sent to it after the fact.

Now, I am sure that wasn't the intent of the provision. And, actually, this provision is based on FDA's unreleased compliance policy guide, which was part of the documents that FDA provided in the context of the Oversight and Investigations Subcommittee investigation. FDA has indicated that this guidance was never re-

leased because the NECC meningitis outbreak made the agency rethink its approach.

Can you describe why FDA included this provision in the draft policy guidance? Do you still believe there is some merit in this provision, in the wake of the NECC outbreak?

Dr. WOODCOCK. Well, like the Members here and in the Senate, we are struggling to put some type of quantitative limits on what can be done. And we are working within the framework that existed at the time and still exists.

We have learned a lot since then. And one of the things we have learned is that this approach can be worked around, as you said. And you can do the math on that and see that you can get up to a very large volume of shipping if you are able to receive names back, similar to if you have a 10-day limit or whatever, you are able to get up to a very large volume if you have enough customers. And then that raises the risk up very high.

I don't think we have, you know, the magic answer about how to identify those highest-risk facilities and what characteristics they should have. And we want to work with the Congress on this because it is a difficult line to draw.

But I feel that the 7-day—there is a loophole there that would allow a proliferation, a very large volume of shipping as long as there was receipt of those names. And that would be very difficult for us to enforce. So we go into a pharmacy, we look, there are lists of names. You know, what are we going to do then?

It really puts the onus, actually, the way I think the bill is drafted, on whoever receives the stuff to send it back, to kind of promise to send the names back in 7 days.

Mr. WAXMAN. It appears to me that you are operating within the confines of the current statutory framework and doing the best you could under that regime. Now, you have suggested that Congress should enact an updated statutory framework that would be better tailored to this new class of large compounding companies.

If we adopt a framework like the one you have described, do you think this 7-day reconciliation provision is still necessary or useful in some way?

Dr. WOODCOCK. It depends on probably how the definition of "traditional compounding" is taken forward. Because we feel that for the large-volume outsourcers, they are really not getting prescriptions. That is not the business they are in. As I said, much of their business is doing what the hospital pharmacies did in their pharmacy years ago. And that has been outsourced—that is why we call them outsourcers—to larger facilities.

Mr. WAXMAN. Are you worried, though, that this 7-day provision might become a loophole?

Dr. WOODCOCK. Well, it could be a loophole. It absolutely could be a loophole. And so I think, collectively, we have to think very clearly about how we draw those lines so that something like NECC does not happen again.

Mr. WAXMAN. Yes. OK. Thank you.

Mr. PITTS. The chair thanks the gentleman and now recognizes the gentleman from Virginia, Mr. Griffith, for 5 minutes for questions.

Mr. GRIFFITH. Thank you, Mr. Chairman. I appreciate that very much.

Let's talk about this 7-day issue and related to the volume. One of the frustrations that we have had with some other folks is that we have actually been asking—and you will see some blanks in the bill, because we are trying to sort that out, which is why sometimes it is nice to have hearings and you can ask these questions in public.

We are trying to figure out at what volume do you all consider them to be large enough that they ought to be considered manufacturers, no matter what they call themselves, that they are, in fact, manufacturers.

And what I have heard from your testimony today is, you said that under the bill, you know, there could be 5,000 to 10,000 vials a week being sent out, and that is too much. So now we have a number at least of 250,000 a year. I multiplied it by 50 instead of 52, figuring there might be a little break in there somewhere. But we have that minimum of 250,000.

So the question is, we are not trying to just say the 7 days; we are looking for something else that we can identify?

Dr. WOODCOCK. Yes.

Mr. GRIFFITH. Crossing States lines doesn't do it, because in my district, I have two cities that are shared, Bristol, Virginia/Tennessee, Bluefield, Virginia/West Virginia, and all kinds of places where the lines—you know, you can get from West Virginia, Kentucky, Tennessee, and North Carolina all in the span of about an hour and a half if you drive the right routes. And so, you know, saying that just crossing the State line won't do it.

So we are looking for some help from you all as the experts. And you indicated that is a difficult line to draw. And I understand that, but we have to draw it. And I think it is our responsibility, with your help, to draw that line.

So I would say to you, do you have an answer to that question today? And if not today, can you give me one?

Because if the right number is, if you produce more than 20,000 vials, then I think we have something we can work with and we can discuss. And I understand you may not be able to give me an exact answer today, but I think that is part of what we need.

Because Congressman Waxman is absolutely right; I don't think 7 days, acting alone, works. With a volume or some other qualifier and the 7 days—the 7 days is to make sure we don't put everybody out of business who is trying to do it right. But the volume number would really help us a lot.

Or if you have some other fix that works besides, you know, just crossing over State lines when you have small-town pharmacies that could be hit when they are in a split city. What do you say to that, and what can you help us on?

Dr. WOODCOCK. Well, we—

Mr. GRIFFITH. We are just trying to get this thing worked out and do it right.

Dr. WOODCOCK. Yes. We would really like to work with you. Any number that we come up with, any set of limits, have challenges, right, as far as how they are defined. The existing—

Mr. GRIFFITH. But here is the problem: We are not going to get it perfect. We——

Dr. WOODCOCK. Right.

Mr. GRIFFITH [continuing]. Are never going to get it perfect. But, you know, in that football field analogy, let's get it 80, 90 yards down the field. Then we can start worrying about how we get the last 10 yards. Right now we don't have any yards on that.

And I am just trying to, you know, solve a problem. And let's not throw out the really good, trying to get to the perfect.

Dr. WOODCOCK. Well, the traditional definition of "compounding," the number is one. I would just like to make that very clear. It is a pharmacist compounding in response to a prescription for an individual patient need.

So, as we get above one, we start going into practices that are batch manufacturing, basically. And what your pharmacy community will probably say is, well, we like to do that because we have multiple——

Mr. GRIFFITH. It is not just the pharmacies. It is the docs and some of the hospitals.

Dr. WOODCOCK. Yes.

Mr. GRIFFITH. Because if you are an ophthalmologist and you need those drugs, if you have an emergency eye surgery going on and you need something right away, you can't wait for it to be compounded up, so you do want to have a supply.

Now, in that regard, as well, you know, we are looking for some help on that number. If 120 days is just picked out of the air and it is the wrong number, help us find the right number for how long, you know, these drugs have a shelf life, or give us some guidelines on how we figure that out.

Because, again, we are not trying to make it hard on anybody. We want the ophthalmologist to be able to provide emergency services. We want the hospitals to be able to have what they need there. But we also want the safeguards that the American public expects and it has a right to expect when we are doing something this complicated.

Dr. WOODCOCK. Well, with regard to the stability numbers or the shelf-life numbers, all right, for pharmaceuticals, those are generated using the actual product and doing actual testing. So then we have a hard number; we know how long it is stable, whether it deteriorates with the stopper that is used and, you know, the degree of the bacterial contamination and so forth, which is not supposed to be in there anyway.

So, other than doing testing like that, you are going to need a very short shelf life to retain confidence that the products are still good.

Mr. GRIFFITH. And I think that is something that we can work out, is a short shelf life. If you can give us some help on what that should be, whether it is 10 days or 20 days. As long as the hospitals and the people doing those emergency surgeries know, then they can adapt to that. But, you know, that is one of those issues that we are trying to figure out.

You know, I know this is difficult, and I really appreciate the work that you have done and the fact that you have given us what

I believe to be very clear and honest answers. But sometimes we have to pull the trigger and figure out what the numbers are.

Dr. WOODCOCK. Yes, we do have to act.

Mr. GRIFFITH. So if you could help us with that, I would greatly appreciate it.

This is not, as you know, a Republican or a Democrat issue. This is just trying to get it right.

But I do agree with Dr. Burgess that we can clarify but I don't think that there is new authority that is needed. But clarifying the authority that we believe exists will help you, will it not? And we only have time for a "yes" or "no."

Dr. WOODCOCK. Yes.

Mr. GRIFFITH. All right. I appreciate that and yield back.

Thank you, Mr. Chairman.

Mr. WAXMAN. Mr. Chairman, may I ask unanimous consent—

Dr. WOODCOCK. Without objection, so ordered.

Mr. WAXMAN [continuing]. To submit a statement?

Mr. GRIFFITH. And, Mr. Chairman, I did, likewise, forget to do a unanimous consent on a couple of documents, if I might.

Mr. PITTS. Without objection, so ordered.

[The information appears at the conclusion of the hearing.]

Mr. WAXMAN. And I have a document also. And I also wanted to thank Mr. Griffith for his willingness to talk this through and work it out.

Mr. PITTS. All right. At this time, the chair recognizes the ranking member emeritus, Mr. Dingell, for 5 minutes for questions.

Mr. DINGELL. Mr. Chairman, thank you. I commend you for holding this hearing.

Dr. Woodcock, welcome. My questions will require "yes" or "no" answers.

Nearly 9 months after the initial outbreak of fungal meningitis from contaminated steroid injections at New England Compounding Center, it is clear to me that Food and Drug needs strong and clear authority over compounding pharmacies, which it now lacks.

My home State of Michigan has been especially hard-hit. To date, there have been 264 cases related to NECC and 17 deaths in Michigan alone, the most in the Nation.

I am confident we can come together in a bipartisan manner to clarify and strengthen the authority of FDA over compounding pharmacies.

Today we have three bills before us which take different responses and answers to solving the problem. Each has its strengths and weaknesses. I am going to focus my questions on important authorities that I believe should be included.

Question one: Does FDA believe that classifying an entity according to the existing statutory scheme of either a traditional compounding pharmacy or a conventional drug manufacturer could cause disruptions in our healthcare system, yes or no?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Does FDA have the authority to require all compounding pharmacies to register with the agency, yes or no?

Dr. WOODCOCK. No.

Mr. DINGELL. No?

Dr. WOODCOCK. No.

Mr. DINGELL. Would you submit for the record what authority you need?

Dr. WOODCOCK. Certainly.

Mr. DINGELL. Does FDA have authority to require all compounding pharmacies to report adverse events, yes or no?

Dr. WOODCOCK. No.

Mr. DINGELL. Does it need that authority?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Submit to us, please, what you think you need, for the purposes of the record.

Does the FDA have the authority to require all compounding pharmacies to follow good manufacturing practices, yes or no?

Dr. WOODCOCK. No.

Mr. DINGELL. Do you need it, yes or no?

Dr. WOODCOCK. "All" might be an overstatement. Yes, for some.

Mr. DINGELL. All right. I would like to have you define what it is you happen to feel you have need of.

Does FDA believe nontraditional compounders should be subject to appropriate good manufacturing practices like manufacturers are, yes or no?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Please elaborate for the record.

Dr. WOODCOCK. Certainly.

Mr. DINGELL. Does FDA believe a risk-based inspection schedule is appropriate for nontraditional compounders, yes or no?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Tell us why for the record, if you please.

Next question: Does FDA have full authority to see all records when inspecting any compounding pharmacy, yes or no?

Dr. WOODCOCK. No.

Mr. DINGELL. Does it need it?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Please define for the record what you think you have need of.

Has FDA faced litigation regarding its ability to inspect records in pharmacies, yes or no?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Please describe for the record what you feel you have need of.

Now, do you need this authority to effectively regulate compounding pharmacies, yes or no?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Please state why for the record.

I have long believed that we must provide agencies like FDA with the necessary authorities and researchers and resources to properly protect public health. FDA has a user-fee system for the approval of pharmaceuticals and medical devices, amongst others. If we give FDA increased authority in this area, which I believe we should, then I believe we should also have a stronger user-fee program.

Now, would the user-fee provisions contained in the Senate bill provide FDA with the necessary resources to carry out these authorities, yes or no?

Dr. WOODCOCK. Yes.

Mr. DINGELL. Would you discuss for the record, please?

Now, the American people deserve a response to the NECC outbreak so that we can ensure that this never happens again. I am committed, like most of my colleagues here, to seeing to it that we work towards a proper bipartisan solution to the problem. And I plan on continuing my discussions with my friends on both sides of the aisle until we reach agreement on the best way forward.

I would like to have you discuss a little further some of the comments that you made in response to Mr. Griffith's rather excellent questions.

I have a curiosity. Is the number of shipments by the compounder as important as to whom they are shipped and what the compounding might happen to be and who the individual is that is making the shipments?

Dr. WOODCOCK. We feel that the highest risk relates to sterile products. So that is number one. Things are going to be injected into your body, right? And the contamination, that—

Mr. DINGELL. So you need authority to define those things, don't they?

Dr. WOODCOCK. That is one.

We propose using interstate commerce as a proxy for risk, because if you are shipping all over the country, you are making more, it is taking longer, right? So the shelf life is going to be longer, and there is time for bacteria or fungi to grow and so forth. And your batches are probably larger, and that increases the risk of errors, and, also, it just simply increases the number of people who could be harmed.

Mr. DINGELL. I am running out of time. And out of respect for my colleagues, would you please submit for the record a statement on this particular point?

Dr. WOODCOCK. Certainly.

Mr. DINGELL. Thank you.

Thank you, Mr. Chairman.

Mr. PITTS. The chair thanks the gentleman and now recognizes the gentlelady from Tennessee, Ms. Blackburn, for 5 minutes for questions.

Mrs. BLACKBURN. Thank you, Mr. Chairman.

And thank you for being with us. We appreciate your time and coming back. I know that you probably and your staff probably feels like we have talked about this issue nonstop, but it is of tremendous concern to us. For those of us in Tennessee, it is especially concerning. We have 14 individuals that lost their lives and so many who are still suffering.

And I will just associate myself with Mr. Burgess's remarks in regard to it being a collective failure. We do realize that there were actions that you all should have and could have taken, and it is of concern to us.

A couple of things I just want to ask you about. Looking at drug shortages, are there any instances where FDA is permitting compounding pharmacies to make products on that drug-shortage list without having those facilities go through the inspections and qualifications?

And, then, are there people that are on the ANDA list that have submitted those applications where you have not gotten around to approving those applications?

Dr. WOODCOCK. Well, first of all, we prioritize any generic drug application that is related to a shortage and try to get it through the process as quickly as possible.

As far as compounding pharmacies, yes, they are making drugs to address shortage issues, but, no, we have no real oversight of that right now. That is not the scheme that is in place. That is regulated primarily by the State boards of pharmacy.

Mrs. BLACKBURN. OK. On the ANDAs, you said you prioritize those applications. How long does it take to get one of those through the process?

Dr. WOODCOCK. Well, it varies tremendously, whether or not the application is in good shape. If there are multiple foreign facilities involved in production of the drug that we haven't inspected before, we may have to go to other countries and inspect those facilities. So that sometimes can be a rate limiting step.

Mrs. BLACKBURN. On average.

Dr. WOODCOCK. I could get back to you on that. I don't have it.

Mrs. BLACKBURN. OK. I would love that. I think that it would be instructive to us.

Mr. Griffith mentioned something about limitations. I understand that many States have used some form of volume limitation for anticipatory compounding to determine whether an entity is acting within the scope of their license.

So do you think that a volume limitation in conjunction with other factors from 503(a) could help distinguish between entities that are engaged in large-scale compounding similar to manufacturing or in traditional compounding?

Dr. WOODCOCK. It is possible. The States have a patchwork of laws which are different. Some allow anticipatory compounding; some allow office stock. So there are a variety of interpretations or laws across the different States.

Clearly, volume is another proxy for risk. And the larger the volume of the batch or lot you are making, the higher the risk that is imposed if you are not using good manufacturing practices.

So that is possible, but we have struggled with this, and we have had a very difficult time coming up with a coherent scheme that would use volume. And then that would have to be usually enforced by the States, because it would apply to all the compounding pharmacies. It wouldn't be a uniform Federal standard, or it would be very difficult for us to enforce it even if it were, because, as the testimony shows, there may be 23,000 pharmacies or something that are doing compounding of different types.

Mrs. BLACKBURN. OK. Thank you for that. I would think that volume could be one of those indicators that may be a bit more illuminating as you try to work through this process. It would seem it would be a key indicator.

With that, I will yield back.

Mr. PITTS. The chair thanks the gentlelady and now recognizes the gentlelady from the Virgin Islands, Dr. Christensen, for 5 minutes for her questions.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman.

And welcome back, Dr. Woodcock.

Dr. WOODCOCK. Thank you.

Mrs. CHRISTENSEN. Some of these questions have been asked one way or another, but I want to just to be clear. And I would like to talk about one of the concerns we have been hearing a lot about, having to do with the proposed statutory framework.

As has been said, FDA has suggested that Congress should revise its statute to clearly delineate which compounding entities should be subject to Federal oversight and which ones should remain the purview of States. Specifically, you have recommended that facilities be subject to FDA oversight if they conduct sterile compounding, which you said is the highest risk; second, whether they compound medicines in advance of or without a prescription, which I don't understand; or if they ship compound medicines across State lines.

One of the problems, according to some of the stakeholders, is that this construct would prevent doctors' offices from obtaining limited amounts of compounded medication without a prescription that would be kept as office stock. So they feel that these medicines need to be in their office so that they can be given to a patient who needs them right then.

It is my understanding from your answers that FDA doesn't support this. So could you explain the rationale for not allowing some limited amount of office stock to be exempt from the triad of requirements?

Dr. WOODCOCK. Certainly.

We are not—we aren't wedded to anything. We need to find a workable scheme, right? Each doctor's office or clinic may say, as I said, they may say, we only use 25 of these vials a week. OK? But if the compounding pharmacy has 1,000 customers, right, then that is 25,000 vials. And would you say that is too many?

So if you simply use that and allow a certain amount of anticipatory office stock, that is what you could end up with. And so you just have to kind of play out this scenario in your mind and what this would look like. And I don't know, maybe you think that them making 25,000 sterile vials is OK, is not manufacturing, right?

Mrs. CHRISTENSEN. I think that anything that goes beyond a specific compound for a specific patient is too much, trust me. And—

Dr. WOODCOCK. Could I say one more thing?

Mrs. CHRISTENSEN. Sure.

Dr. WOODCOCK. We are not proposing that this be prohibited. We are saying that it should go into a category that involves good manufacturing practices so that there would be oversight of the aseptic processing so that we would be assured it would be done correctly and at least these products would not be contaminated.

Mrs. CHRISTENSEN. Got it. And are there certain types of compounded drugs for which some limited amount would not be subject to the limitation? Are there specific drugs that you could conceive of that could be compounded without—for which some limited amount should not be subject to the extra oversight?

Dr. WOODCOCK. Well, we have proposed that the category of federally regulated would be, you know, interstate commerce without a prescription of sterile drugs, right? And that leaves a large variety of other things to the States, including intrastate sterile drugs,

which still, arguably, can be of high risk, and all other compounded products, which would be the oral, the creams, the lotions, all those sorts of things.

Now we have proposed that there be a floor that you should not be able to compound drugs, say, that FDA pulled off the market because they weren't safe, OK, and that you shouldn't compound drugs from a monograph, you know, from an appropriate source OK, and so forth. So we had certain criteria we think should apply to all pharmacies who compound. However that vast majority of non-sterile, non-injectables so we really are not proposing to have under this broad scheme, this new scheme that we were talking about.

Mrs. CHRISTENSEN. And are there any exemptions to the across State line borders for pharmacies that are close to State borders or that routinely operate across State borders today?

Dr. WOODCOCK. Right, well that is, I think, the question that we just heard that that creates some unfairness like any scheme we are going to apply there would be some disparities. We weren't proposing that there would be that exemption for States that were close by or four corners or whatever.

Mrs. CHRISTENSEN. The question has been raised that you all had a lot of authority that you hadn't exercised before so, and you said that FDA took some aggressive action and when you have taken that aggressive action, is it that FDA has gone over on a limb in the interests of public health risking court challenges? Or did you find some authority that you didn't think you had before?

Dr. WOODCOCK. Well, as I said, we, I think we may get court challenges. I think in some cases, the States have taken action because we have brought this to their attention, and they are the holders of the, you know, they issue the pharmacy licenses. And so although we have even inspected 61 pharmacies, now if you think of the universe that we are talking about, it is a much larger universe, and new ones can grow up all the time.

So although we are taking aggressive action, the fact that we do have to think through the judicial consequences and so forth meaning each of these actions, as I would call them pretty lawyer intensive, all right, and we don't have unlimited legal resources.

Mrs. CHRISTENSEN. I have gone over my time, thank you.

Mr. PITTS. The chair thanks the gentlelady and now recognizes the gentlelady from North Carolina, Mrs. Ellmers, for 5 minutes for questions.

Mrs. ELLMERS. Thank you, Mr. Chairman, and thank you, Dr. Woodcock, for being with us again.

To the best of my knowledge this is about the fourth hearing that we have had in the subcommittee on this issue, especially in relation to the New England Compounding Center, and I think there are still some questions out there that many of us have about how that process is moving forward.

It seems to me, after looking at all the information that the FDA did have some authority at that point to shut down NECC, and of course, that is not the possess that went forward and we obviously need to clarify, of course, the FDA authority as been discussed many times here already today.

Dr. Woodcock, in your opinion, would you agree with my statement and might you have anything to add? What can we do to

bridge this? Because as we are having this conversation, there are many times that you say that we did have authority, we did not have authority, but we have got to fix this problem. So what is your solution? What do you want to see done?

Dr. WOODCOCK. Well, what FDA has proposed is that we have different legislation, I won't say it is quote, that the large scale industry that has grown up especially that is making sterile products be subject to Federal regulation. It is basically a new type of industry, the scale, the fact that it is sterile and so forth, and it is not the traditional corner drugstore making—

Mrs. ELLMERS. And that, I guess at that point is now where we have the question of the amount that is being compounded, meaning each individual vial, or, you know, sterile unit, I know I have heard shelf life be discussed, and of course, I think that does have more to do with the actual make-up of the compounded prescription, which leads me again to the question, I know when we have a traditional pharmacy, we have a prescription, and that is filled for the patient. Then we, as you pointed out have this situation where we have hospitals and different, you know, maybe outpatient surgery clinics that use those compounded products as well.

Why can't—I guess my question is rather than concentrating so much on the number, obviously there is a safety issue there, we want to make sure we are producing a sterile product, but when it comes to going to a hospital or an outpatient surgery center, why can it not stay under the same category that it is right now rather than moving into a larger manufacturing label or status?

Dr. WOODCOCK. Because they make—the people who supply these outpatient clinics like NECC, OK, make large scale volume, which Dr. Burgess has said, well, that clearly is manufacturing, we know it when we see it, right, the question is how do you distinguish that.

Mrs. ELLMERS. Well, and that leads me to my next thought, and I realize that we are talking about legislation that is already being proposed, but if we know that an outpatient clinic does a number, a particularly an average number of cases every month, and they were to receive that compounding product for that amount, would that not essentially be kind of a large-scale prescription when you think about it? Is there not another avenue we can take here rather than just add more regulation and more costs, but at the same time, continue to produce a very safe product?

Dr. WOODCOCK. Well, that is the issue, continuing to produce a safe product. As I said, we have had another outbreak since the last time this body had a hearing, all right.

Mrs. ELLMERS. I am going to stop you there, thank you, I do have about 50 seconds which leads me to my next question. At the time of the outbreak, the NECC outbreak, there was a compliance policy guide that the FDA was preparing, but I think that had been put on hold.

Has that now been, has that policy been evaluated? And what is the FDA doing?

Dr. WOODCOCK. We have learned since then, and as I told Dr. Burgess we are aggressively applying our existing authorities under the law to these pharmacies. Existing authorities require prescriptions.

Mrs. ELLMERS. So the question, again, is has the agency evaluated the compliance policy guide? Has that been——

Dr. WOODCOCK. Yes.

Mrs. ELLMERS. Is that being implemented now as this authority?

Dr. WOODCOCK. No, we feel that parts of that are actually unfeasible based on what we have learned. We have learnt a lot since the NECC outbreak all right and we have revised our approach to be more practical.

Mrs. ELLMERS. Thank you and my time has run out thank you.

Mr. PITTS. The chair thanks the gentlelady. I recognize the gentlelady from Illinois, Ms. Schakowsky 5 minutes for questions.

Ms. SCHAKOWSKY. I am over here, Dr. Woodcock.

Dr. WOODCOCK. I am sorry.

Ms. SCHAKOWSKY. Did I hear you at some point say that there ought to be labels of dates certain and information for the consumer on compounded products?

Dr. WOODCOCK. Yes, after this NECC outbreak, many of the FDA staff who had to go in the hospital they said, well, we don't even know what products we are getting that are compounded when they are having a procedure or something. There is no label that is required now that identifies a product as a compounded product.

Ms. SCHAKOWSKY. Here is my question problem, that I began my activism decades ago to get expiration dates on products sold in the supermarket. I am for consumer information. But when it comes to prescription drug, particularly if you are in the hospital, are you suggesting that in some way, we leave this up to an informed consumer to be able to make decisions on whether or not they want that or that it be suitable for them?

Dr. WOODCOCK. Not really. We think that this simply raises awareness about the use of compounded drugs. The use of, there are beyond use dates on compounded products now. Our issue with them is that they aren't based on evidence, based on experiments that are done on that compounded product from what we have seen in our inspection.

Ms. SCHAKOWSKY. Well, let me ask you about all the prescriptions that we get. They all now have a date on them and I regularly go through my shelf and dispose of——

Dr. WOODCOCK. Excellent.

Ms. SCHAKOWSKY. Outdated drugs. Are all of those, do we know that those are accurate?

Dr. WOODCOCK. Absolutely. They have to perform experiments on stability and dating period and submit all that information to FDA and we have to agree with it.

Ms. SCHAKOWSKY. OK, so that is not part of the requirement and something that you would need the authority to require that?

Dr. WOODCOCK. Performing stability testing, so forth, on products is part of good manufacturing practices.

Ms. SCHAKOWSKY. And so that would, under your new categories, would be required of these compounders?

Dr. WOODCOCK. We are proposing that for the highest risk facilities that make sterile drug products and ship them inter State.

Ms. SCHAKOWSKY. So if we are not doing it by quantity, what are we doing it by? What do you recommend we do it by?

Dr. WOODCOCK. We propose by risk and simply pulling off the highest risk class of products which is the sterile products that are shipped inter State so they are going, causing multi State outbreaks, and that are without a prescription and the prescription—without a prescription is a proxy for mass production, OK, because it is not one pharmacy making one sterile product for a person, say, in another State. They are making large batches and then shipping them all around.

Ms. SCHAKOWSKY. So the FDA has talked a lot about medical need as a condition for compounding a product. So how should we incorporate this concept into legislation?

Dr. WOODCOCK. We feel that is a fundamental concept for compounding. It is the reason—why else would you give people products that didn't go through the system that Congress has established for drugs, right, which is they are tested for safety and efficacy, and they have applications and everything, and the reason is there is a medical need that is not met by existing products. And so we feel to raise practitioners' awareness that they would indicate that there was a medical need for this product, and why are we doing this? Because when we talk to people who bought products from NECC, the practitioners, what they said, well, there was just the order form online, and we just ordered like any other order that you would make. And so there was no awareness, there was no practitioner awareness that this was a higher risk product.

Ms. SCHAKOWSKY. I see. In your testimony, you explain that certain products with limited exceptions are not appropriate for compounding under any circumstances. Would you include this situation that we are just talking about, that, you know, the practitioner just went online, found this to be available? Should those products not have been compounded under any circumstances?

Dr. WOODCOCK. No, we have very specific criteria for what we think shouldn't be compounded under any circumstances, and that would be, for example, the drugs that FDA has pulled off the market because they dangerous. We don't think they should be compounded. Very complex dosage forms, our, the pharmaceutical manufacturers have trouble making certain dosage forms right. For example, extended release may cause dose dumping and get all the dose in the body at once and could kill you, for example, and they have to do extensive testing on their products to make sure they have been manufactured correctly. So we don't think some of these very risky products should be compounded either.

Ms. SCHAKOWSKY. Thank you. I appreciate it. I yield back.

Mr. PITTS. The chair thanks the gentlelady and now recognizes the gentleman from Florida, Mr. Bilirakis, 5 minutes for questioning.

Mr. BILIRAKIS. Thank you, Mr. Chairman I appreciate it very much. Thank you for your testimony. Dr. Woodcock, you mentioned that copies of FDA-approved drugs should never be compounded. What about the drug progesterone, which, for years, was compounded by pharmacists for pregnant women to prevent premature births? In 2011, FDA approved Makena, which is a manufactured form of progesterone. The manufacturer sent a cease and desist letter to compound pharmacies, and FDA weighed in and said phar-

macies could continue to compound this drug even though a more expensive manufactured drug is available.

If we explicitly prevent compound pharmacies from making copies of FDA-approved drugs, what will happen to pregnant women's access to achieve drugs, affordable medication to prevent premature births?

Dr. WOODCOCK. You know, I can't comment specifically on that instance because of ongoing litigation issues. However, I think in general, Congress set up a system that required new drugs to go through the FDA review process, and that was because of the many abuses and many deaths and many problems there were long ago when there wasn't a system to make sure drugs are safe and effective. So there were many outbreaks in the past as well as like the thalidomide crisis and so forth, all of which led Congress to do this.

Now, if we feel, in general, if there is a safe and effective drug available to the public, people should not be exposed to drugs that are of lower quality unless there is a medical need for that other product.

Mr. BILIRAKIS. Next question, you mentioned needing the power to access pharmacy records. Are you looking for the authority over pharmacy records in general, or just the nontraditional compound pharmacies?

Dr. WOODCOCK. Well, we would like to, so to speak, be able to distinguish, more or less, the sheep from the goats. We need to know, people have said, well, why don't you act on this or that or other, haven't we acted if we can't demonstrate that a pharmacy is shipping large quantities of drugs that violate whatever scheme Congress comes up with, right, then we won't have the power to use our authorities. And the way we do that, you look at their shipping records and say if there is a requirement for names or prescriptions, we would need to be able to verify that, otherwise we—there are bad actors out there and there are people who say oh get all that stuff or we don't do this, and if we can't verify that then it really ties our hands.

Mr. BILIRAKIS. How about, you mentioned using the administrative warrants to compel access to records.

Can you explain what this process is and how do you go about getting the records, the warrants?

Dr. WOODCOCK. Well, I am not a lawyer, all right. But my understanding, I have asked the lawyers and we have to go to a court and we have to ask the court. And sometimes it can be done rapidly, but often it averages about 2 weeks. And we are concerned, first of all, of course, if there is an outbreak, that is too long because lives are at stake.

Another thing, a problem we can have is that people can clean up and destroy their records in the time that it takes for us, and, of course, we don't have evidence that they have destroyed records because they may be destroyed, but when our investigators are in some of these firms, they have had a very strong smell of bleach which we think means that the mold has been bleached off of the counters and so forth, and that there was a lot of cleanup during the time we went and tried to get a warrant to get in.

Mr. BILIRAKIS. Thank you. We all, of course, want to ensure the safety and sterility of compounded drugs. We must also not lose the

sight of the important role that compounded drugs play in patient care. Some physicians keep a supply of compounded drugs available for anticipatory office use because in waiting for the drug to get compounded for the patient, that waiting period could endanger the patient's health. I know we touched about upon this, but some of the bills we are reviewing today include patient specific prescription requirements for certain compounded drugs.

Do these prescription requirements really address and improve the safety and sterility of compounded drugs? Are there other measures that can be taken to improve the safety of these products that also ensure physician and patient access to compounded drugs for use in the office setting?

Dr. WOODCOCK. Well, our proposal doesn't preclude lack of prescriptions in the anticipatory compounding. What we are saying is when you do that for sterile products, you should make the products under good manufacturing practices, proper aseptic processing so you don't contaminate them. Now, that is one way to deal with this. That is what we are proposing is if you wish to ship products, sterile products around and not get prescriptions, then you should make them under good manufacturing practices because you are likely to be making batches of sterile products, and that really doesn't look like compounding, it looks more like manufacturing when you are making batches.

Mr. BILIRAKIS. Thank you, Mr. Chairman. I yield back.

Mr. PITTS. The chair thanks the gentleman and now recognizes the gentlelady from Florida, Ms. Castor, 5 minutes for questions.

Ms. CASTOR. Thank you, Mr. Chairman, and thank you Dr. Woodcock for being here. The last time you were here you were kind of to allow me to change the subject and ask you about one of the serious drug shortages facing our country, and that involves the injectables, injectable nutrition that primarily affects premature infants and our children's hospitals continue to raise the issue and practitioners and scared parents across the country. I know at the end of May, FDA acted to allow some imports of those nutrition elements.

Can you give us an update on how it is going? Is the situation improving? Have you hit any roadblocks.

Dr. WOODCOCK. It took longer than we had hoped and when I talk to you last, I thought it was imminent and it took longer than what we hoped to get those products in. We believe we are alleviating these shortages, but we are not out of the woods yet. We do not have a U.S. manufacturer online to my knowledge that can give us a stable supply but we are working on that.

Ms. CASTOR. Are there prospects for U.S. manufacturers to come online?

Dr. WOODCOCK. That is what we believe, yes.

Ms. CASTOR. And what would that time frame would be?

Dr. WOODCOCK. Pardon me.

Ms. CASTOR. What do you think the time frame would be?

Dr. WOODCOCK. I don't know. We can get back to you with details if you would like.

Ms. CASTOR. Good. I look forward to that, thank you very much. And you really have clarified over the number of hearings that we have had back on this topic on reforming drug compounding, we

have had a series of hearings, and your message is sinking in, I believe. We now have three bills that are out there, you have got a Senate bill by Senator Harkin, you have got one that is kind of on the other end of the spectrum by former Representative Markey, you have Mr. Griffith's bill now that he is working on.

When you look at the three bills that have been drafted, can you point to a section of any of those bills that you say boy, that is really the most important thing that could be accomplished here or that would be one of our priorities going forward for FDA and protection of the public health?

Dr. WOODCOCK. Well, we do feel the Senate bill has the right framework. There is still issues about, but you know it does provide registration so we can find out who the people are, it provides reporting of adverse events so that if any compounding pharmacy starts getting into trouble, we can react quickly. It does have a user fee program, it does carve out a section of a sterile manufacturers who would be subject to higher standards and it does provide some other Federal standards. So we feel that is a good start, but all—this is a very difficult issue to draw these lines correctly and they are trade-offs that have to be made, and we recognize that everyone is struggling with this and we want to work with you all.

Ms. CASTOR. In that Senate bill, is it clear to you when you read it that the traditional neighborhood pharmacist that are not in the, not making thousands of batches or even hundreds of batches are clearly exempt.

Dr. WOODCOCK. Yes, the Senate bill has State law prevail on the traditional pharmacy compounding, and we feel, unfortunately, there is a bit of a patchwork there because each State has a different set of laws, so your two pharmacies are 20 miles apart in different States may be operating under totally different frameworks, and we think that will be difficult for us to enforce, pending one might be regulated by us, and the other on the other State regulated by the State, and that is very difficult.

Ms. CASTOR. Well, thank you very much. I was thinking about this earlier today reading over the testimonies and I think if we just put ourselves in the shoes of the average American consumer, I think what they want most of all is to be assured that especially the highest-risk drugs, the ones that are being injected, like you said, are being manufactured in a way that is safe and that the government at least has the authority to know who they are, where they are, so that we can ensure that no one is harmed to the extent of what happened with NECC. So thank you very much. I yield back.

Dr. WOODCOCK. Thank you.

Mr. PITTS. The chair thanks the gentlelady and recognizes the gentleman from New Jersey, Mr. Lance, for 5 minutes for questions.

Mr. LANCE. Thank you, Mr. Chairman.

Dr. Woodcock, your opinion should entities making nonsterile products in advance of prescription shipping interstate be regulated by the FDA as traditional manufacturers or by States as traditional compounders?

Dr. WOODCOCK. So should traditional, should manufacturers who are making nonsterile products and shipping them interstate.

Mr. LANCE. Interstate?

Dr. WOODCOCK. Interstate, perhaps in very large quantities be regulated as manufacturers or.

Mr. LANCE. Or as traditional compounders.

Dr. WOODCOCK. I think that is a policy call. There are trade-offs there; there are is far more of that. These are lower risk products, and what we have proposed is other restrictions like not copying FDA-approved product and only working from certain bulk product, API's and so forth, that would put some boundaries on these practices but I think there is some danger of folks going into business as a kind of shadow generic company without FDA oversight, if they could ship broadly.

Mr. LANCE. If they were regulated under the FDA what would the proposed framework be? As opposed to being regulated by the States.

Dr. WOODCOCK. Well, we haven't proposed anything for that group. Generally speaking, doing those practices, you would have to, right now under the current law, which we have been talking about, you have to file an application for every single form that you are shipping, and often, of course, these are customized to different doctors' preferences and so forth, and these groups make thousands of different dosage forms, they would have to file an application for each one with extensive documentation and pay user fees.

Mr. LANCE. Thank you. I know that you have recently conducted a series of inspections compounding pharmacies and as I understand it, you have done that in conjunction with State officials; is that accurate, Dr. Woodcock?

Dr. WOODCOCK. Yes, in almost all cases, we have gone in with the State.

Mr. LANCE. And you have stated that the agency needs full record inspections authority for every pharmacy in the country and in that, if you are conducting these inspections with State Pharmacy Board officials, do you believe as well that you need independent authority independent from the State boards?

Dr. WOODCOCK. We have had some cases where the State officials, due to resource constraints, have not been able to go in with us and we are concerned that might be even more happen more often in emergency where we feel that we really need the ability to get in there. We do always try to have the State officials come with us because they have we have joint authorities.

Mr. LANCE. Are some States better at this than others traditionally, or does it just vary based upon State resources at the moment.

Dr. WOODCOCK. I don't think we have a large enough sample size to say which States, you know, we know some States as the Board of Pharmacy Association has testified, some States are better staffed and so forth than others for their board of pharmacy operations.

Mr. LANCE. Thank you. I would be happy to yield to any other member who wishes to speak.

Mr. GREEN. If I could, we are looking, and I think I share it with my colleague, Congressman Griffith, we are looking at multiple things that gives the FDA the authority to do it, because we don't

want this to happen again, and I have to admit having served there a good while, that first hearing we had neither the FDA nor the compounders nor the State agencies showed that they were actually do the doing the job, so we want to make sure you have the tools, so it will be multiple and I would be glad to my colleague from New Jersey to yield to my colleague, Mr. Griffith.

Mr. GRIFFITH. If I could have a minute of that time I would appreciate it, and one of the things we are also working on in the bill that I think is helpful and I think you would agree is that we set up a facilitating process where there are complaints from the State where they can work a little more efficiently with the FDA, and likewise, if you hear something go on from State A that the FDA can then communicate that it to that to State B and C, that this particular group may be having a problem.

Dr. WOODCOCK. Yes, we would like to have, perhaps, a message board or something but we don't want to turn into the telephone operator.

Mr. GRIFFITH. I understand that, but anything we can do to facilitate, because one of the problems is those who were here for the hearings know is that we had a couple of States that were blowing the whistle, and no action was taken, so we want to try to make sure we facilitate in making sure that the next time when Colorado or Ohio or some other State is, in fact, raising red flags that that message is getting through, and I do appreciate and yield back to—

Mr. LANCE. Thank you very much.

Mr. PITTS. The chair thanks the gentlemen. That concludes questions from the members. I am sure they will have written questions. We ask that you please respond promptly. Dr. Woodcock, as always, you have been a very excellent witness. Thank you for your testimony.

Dr. WOODCOCK. Thank you. I am pleased to respond.

Mr. PITTS. Thank you. I will call the second panel up at this time and introduce them as they come forward. In this order they will testify: Dr. Doug Hoey, chief executive officer, National Community Pharmacists Association; Dr. Kasey Thompson, vice president, American Society of Health-System Pharmacists; Mr. Jeffrey Francer, assistant general counsel, Pharmaceutical Research and Manufacturers of America; Dr. David Gaugh, Senior Vice President for Sciences and Regulatory Affairs, Generic Pharmaceutical Association; Mr. Allan Coukell, Senior Director Medical Programs, the Pew Charitable Trust; Dr. David Miller, Executive Vice President and CEO, International Academy of Compounding Pharmacists; and, finally, Dr. Carmen Catizone, Executive Director, National Association of Boards of Pharmacy.

Thank you all for coming.

You will each have 5 minutes to summarize your testimony. Your written testimony will be placed in the record.

Dr. Hoey, we will start with you for an opening statement.

STATEMENTS OF B. DOUGLAS HOEY, CHIEF EXECUTIVE OFFICER, NATIONAL COMMUNITY PHARMACISTS ASSOCIATION; KASEY THOMPSON, VICE PRESIDENT, AMERICAN SOCIETY OF HEALTH-SYSTEM PHARMACISTS; JEFFREY FRANCER, ASSISTANT GENERAL COUNSEL, PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA; DAVID GAUGH, SENIOR VICE PRESIDENT FOR SCIENCES AND REGULATORY AFFAIRS, GENERIC PHARMACEUTICAL ASSOCIATION; ALLAN COUKELL, SENIOR DIRECTOR, DRUG AND MEDICAL DEVICES, THE PEW CHARITABLE TRUSTS; DAVID G. MILLER, EXECUTIVE VICE PRESIDENT AND CEO, INTERNATIONAL ACADEMY OF COMPOUNDING PHARMACISTS; AND CARMEN CATIZONE, EXECUTIVE DIRECTOR, NATIONAL ASSOCIATION OF BOARDS OF PHARMACY

STATEMENT OF B. DOUGLAS HOEY

Mr. HOEY. Thank you and good afternoon, Chairman Pitts and Vice Chairman Burgess and Ranking Member Pallone, members of the subcommittee, the National Community Pharmacists Association greatly appreciates the opportunity to testify today and share the community pharmacy perspective on legislation addressing pharmacy compounding.

NCPA represents the interests of America's community pharmacists, including the small business owners of more than 23,000 independent community pharmacies.

Almost 86 percent of independent community pharmacies compound medications. Our members perform a wide variety of compounding services, including working with physicians to create medications to help patients needing hormone replacement medications, help pediatric patients, and those with severe nausea and vomiting where commercially available medications are unresponsive or unavailable to give just a few examples.

NCPA commends members of this committee for taking a closer look at what actions and inactions led to the tragic NECC event. We believe this committee has taken the proper steps by focusing on investigations into clarifying existing oversight to ensure that the appropriate regulatory bodies are exercising their full authority.

NCPA is also grateful to Congressman Griffith for the tireless efforts to prevent a tragedy like NECC from occurring again. NCPA supports the approach of Representative Griffith's discussion draft as it is not a broad expansion of FDA power over historically State regulated pharmaceutical compounding. To the contrary, the draft strikes the proper balance of making certain that future tragedies are avoided while also preserving patients' access to vital compounds.

In addition, NCPA fully supports the discussion draft to preserve State Board of Pharmacy oversight of pharmacy compounding. NCPA has historically, and continues to advocate that pharmacy compounding is best regulated by the State Boards of Pharmacy. Conversely, manufacturing is overseen by the FDA. If the FDA has a concern about an appropriately licensed pharmacy, then the FDA currently has the authority to ask the State Board of Pharmacy to work with them to address the issue. NCPA also strongly supports

efforts by Representative Griffith's discussion draft to preserve office use and anticipatory compounding where State laws allow such practices.

In order to preserve access to compounds, the discussion draft acknowledges that pharmacies should not be hindered in their ability to engage in anticipatory compounding as long as it is reasonable and based on a historical pattern of prescriptions, or for specific patients served by that pharmacy.

Furthermore, NCPA strongly supports the efforts of the discussion draft in recognizing that strengthening communication between FDA and State Boards of Pharmacy is essential.

NCPA believes one of the leading contributors to the NECC tragedy was the failure of the FDA to exert its existing authority to oversee entities going beyond pharmacy compounding. Communication and coordination between State Boards of Pharmacy and the FDA is imperative.

While NCPA appreciates all efforts on this very important issue, we do have strong concerns with other legislative proposals, including granting FDA additional authority to create "do not compound" lists.

Contrary to the discussion draft, other legislative proposals grant the FDA unrestricted authority to designate drugs or specific categories of drugs to a "do not compound" list. This would be an unnecessary expansion of FDA authority over the practice of pharmaceutical compounding while doing nothing to prevent another tragedy like NECC.

A second concern is requiring community pharmacies to notify FDA when compounding short supply medications. While the discussion draft adequately addresses the concern that shortages of prescription drugs have tripled during the last 5 years, other legislative proposals place burdensome FDA notification requirements on compounding pharmacies.

Mandating all compounding pharmacies to bypass their State Board of Pharmacy does nothing to prevent another NECC.

And, third, exempting pharmacies within health systems from compounding standards, while the discussion draft holds all compounding pharmacies to the same compounding standards, other legislative proposals exempt all pharmacies within health systems from the proposed compounding requirements.

A recent OIG report found that almost half of hospitals stated that cost and space limitations would be major challenges to achieve USP 797 compliance. Thus, as Congress addresses this very important issue, the intent should be to ensure all patients receive safe and quality compounded medications.

In conclusion, NCPA is committed to working with Members of Congress in order to make certain that a tragedy such as the New England Compounding Center does not occur in the future, while also preserving patients' access to customized and safe compounded medications.

Thank you for inviting NCPA to testify and to share the view points of independent community pharmacy owners and operators across the country on compounding. I look forward to answering any questions you may have. Thank you.

Mr. PITTS. Thank you, Dr. Hoey.

[The prepared statement of Mr. Hoey follows:]

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United States House of Representatives

Committee on Energy and Commerce

Subcommittee on Health

Hearing on “Reforming the Drug Compounding Regulatory Framework”

Tuesday, July 16, 2013

Chairman Pitts, Vice-Chairman Burgess, Ranking Member Pallone and Members of the Subcommittee, the National Community Pharmacists Association (NCPA) greatly appreciates the opportunity to testify today and share the community pharmacy perspective on legislation addressing pharmacy compounding. NCPA represents the interests of America’s community pharmacists, including the small business owners of more than 23,000 independent community pharmacies. According to a NCPA member survey, almost 86% of independent community pharmacies compound medications. Our members perform a wide variety of compounding services including hormone replacement medications, making suspensions palatable for pediatric patients, different dosage forms for patients suffering from intractable nausea and vomiting, and medications for cystic fibrosis patients, to name a few.

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NCPA commends members of this Committee for taking a closer look at what actions and inactions led to the tragic NECC event. This Committee has taken the proper steps to address this tragedy by focusing on investigations into what steps should have been taken and oversight to ensure that the appropriate regulatory bodies are exercising their full authority. NCPA also is grateful to Congressman Griffith for his tireless efforts to prevent a tragedy like NECC from occurring again while also making certain individuals maintain access to their essential compounded medications.

NCPA supports the approach of Rep. Griffith's discussion draft as it is not a broad expansion of FDA power over historically state-regulated pharmaceutical compounding but, to the contrary, strikes a proper balance of making certain that future tragedies are avoided while also preserving patients' access to vital compounds.

Rep. Griffith's Discussion Draft Recognizes the Importance of Compounding

Representative Griffith's discussion draft recognizes that pharmacist compounding is an integral part of the pharmacy profession and meets patients' needs in a variety of care settings. When manufactured drugs aren't an option, independent community pharmacists prepare customized medications for patients in accordance with a prescriber's prescription based on the patient's individual needs.



Rep. Griffith's Discussion Draft Preserves State Board of Pharmacy Oversight

In addition, NCPA fully supports efforts by Rep. Griffith's discussion draft to preserve state Board of Pharmacy oversight of pharmacy compounding. NCPA has always and will continue to advocate that pharmacy compounding is best regulated by the state Boards of Pharmacy while manufacturing is overseen by the FDA. Boards of Pharmacy currently oversee all aspects of pharmacy practice. If the FDA has a concern about an appropriately-licensed pharmacy, then the FDA currently has the authority to ask the state Board of Pharmacy to work with them to address the issue.

Rep. Griffith's Discussion Draft Preserves Office Use and Anticipatory Compounding

NCPA also strongly supports efforts by Rep. Griffith's discussion draft to preserve office use and anticipatory compounding where state laws allow such practices. In order to preserve access to compounds, Rep. Griffith's discussion draft acknowledges that pharmacies should not be hindered in their ability to engage in anticipatory compounding as long as it is reasonable and based on a historical pattern of prescriptions or for specific patients served by that pharmacy. In addition, NCPA supports Rep. Griffith's discussion draft's efforts to preserve the usual and customary practice of compounding for multiple patients receiving the same or similar medications at hospitals, physician offices, and other health entities.



Rep. Griffith's Discussion Draft Increases Communication between the FDA and State Boards of Pharmacy

Furthermore, NCPA strongly supports the efforts of Rep. Griffith's discussion draft in recognizing that strengthening communication between FDA and state Boards of Pharmacy is essential. NCPA believes one of the leading contributors to the NECC tragedy was the failure of the FDA to exert the existing authority it has to oversee entities going beyond pharmacy compounding. Communication and coordination between state boards of pharmacy and the FDA is imperative. Rep. Griffith's draft addresses issues such as that currently, state Boards of Pharmacy have no way of knowing whether FDA has followed up on actions previously taken against an entity. Boards do not know whether the response from an entity being inspected by the FDA addresses all concerns and is sufficient without necessary further action or whether further action is needed.

NCPA has Concerns with other Legislative Proposals

While NCPA appreciates all efforts on this very important issue, NCPA has strong concerns with other legislative proposals including:

(1) Granting FDA additional authority to create "do not compound" lists.

Contrary to Rep. Griffith's discussion draft, other legislative proposals grant FDA unrestricted authority to designate drugs or specific categories of drugs to a "do not



compound” list prohibiting these drugs from being compounded. This proposal could potentially allow FDA to prohibit compounding pharmacies from compounding hormone medications, thyroid preparations, promethazine gels, and medications to treat autism, as several examples. These “do not compound lists” would give FDA overly broad authority to regulate compounding. This would be an unnecessary expansion and overreach of FDA authority over the practice of pharmaceutical compounding while doing nothing to prevent another tragedy like NECC.

(2) Requiring community pharmacies to notify FDA when compounding medications that are in shortage.

While Rep. Griffith’s discussion draft adequately addresses the concern that shortages of prescription drugs have tripled during the last five years and are predicted to continue to increase, other legislative proposals place burdensome FDA notification requirements on compounding pharmacies. NCPA has strong concerns with legislative proposals that purport to preserve oversight of state Boards of Pharmacy over compounding but to the contrary, mandate all compounding pharmacies trying to fill medication gaps during dire times of shortages bypass their state Board to report to the FDA. Shortages result in greater stress on the overall health care system in not only compromising the quality and safety of patient care, but also leading to both direct and indirect increased health care costs. Subjecting compounding pharmacies to over-



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burdensome FDA reporting requirements during times of shortages increases the devastating impact of drug shortages while doing nothing to prevent another NECC tragedy.

(3) Exempting pharmacies within health systems from compounding standards.

While Rep. Griffith's discussion draft holds all compounding pharmacies to the same compounding standards so that patients have assurance that they are receiving the same quality of care regardless of whether the patient receives compounded medications from a hospital or a community pharmacy, other legislative proposals exempt all pharmacies within health systems from the proposed compounding requirements.

NECC's business growth was driven by demand from health systems because these health entities need compounded sterile products -- especially during times of drug shortages. This is alarming as a report released by the Office of Inspector General entitled, *High-Risk Compounded Sterile Preparation and Outsourcing by Hospitals That Use Them*¹, found that while hospitals plan to increase their in-house compounding, almost half of hospitals stated that cost and space limitations would be major challenges to achieve USP 797 compliance. Other hospitals in the report stated that in order to become fully compliant with USP 797, hospitals would be forced to undergo building redesign and new construction.

¹ See OEI-01-13-00150

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Thus, as Congress addresses this very important issue, the intent should be to ensure all patients receive safe and quality compounded medications.

Conclusion

NCPA is committed to working with Members of Congress in order to make certain that a tragedy such as the New England Compounding Center does not occur in the future while also preserving patients' access to customized and safe compounded medications.

Thank you for inviting NCPA to testify and to share the viewpoints of independent community pharmacies across the country on compounding. I look forward to answering any questions that you might have.

Mr. PITTS. Dr. Thompson, you are recognized for 5 minutes for an opening statement.

STATEMENT OF KASEY THOMPSON

Mr. THOMPSON. Good afternoon, and thank you, Chairman Pitts and distinguished members of the committee for holding this hearing. I am here today to provide ASHP's perspective as a professional society that represents over 42,000 pharmacists who practice in hospitals, health systems and ambulatory clinics, and has been a recognized leader for over 20 years in the development of guidelines on sterile compounding, nonsterile compounding and guidelines on working with outsourcers. The event caused by the New England Compounding Center resulted in 61 unnecessary deaths and more than 700 meningitis cases.

ASHP strongly believes that the authority and accountability between the FDA and State Boards of Pharmacy needs to be clarified. We believe that compounding outsourcers that prepare customized sterile preparations that are not commercially available should be held to the highest standards for quality, including relevant current good manufacturing practices and should be required to be registered with and routinely inspected by the FDA.

Further, we believe that these entities should not copy commercially available products except in the cases of drug shortages or to make a medically necessary variation that meets patient specific needs. The drug approval process in the United States is the gold standard and should be maintained as such. However, it is important to recognize that there are many legitimate and medically necessary compounded sterile preparations that simply are not available from a brand or generic manufacturer in the strength or dosage forms that patients need.

U.S. hospitals prepare a vast array of compounded sterile preparations from FDA-approved products every day in order to meet patient-specific needs. The compounded medications that hospitalized patients need range from simple intravenous admixtures to complex customized medications that are not available off the shelf, such as multi-ingredient cardioplegia solutions for heart surgery, epidural pain medications for women in labor and delivery, concentrated pain medications for cancer patients, and adult medications prepared in concentrations that can be safely administered to babies and children.

Where necessary, hospitals enlist the services of qualified compounding outsourcers for some preparations for several reasons. For example, some hospitals may not have the necessary equipment or facilities to prepare some high risk sterile preparations, which is sometimes the case in small and rural hospitals. Or they may face medication shortages for commercial products that can only be replicated by outside suppliers that provide customized compounded sterile preparations. They may also enlist the help of outsourcers to prepare FDA-approved sterile products in ready-to-administer packages in the strength and dosage forms they need.

The evolution of the compounding outsourcing industry over the past decade has outpaced the ability of State and Federal laws to

keep up, creating legal and regulatory gray areas between State and Federal Government.

Unfortunately, it just isn't as simple as calling these large scale anticipatory compounding entities a pharmacy, a repackager or a pharmaceutical manufacturer. They are something in between each of these but no one category fits them perfectly.

Recent bipartisan Senate legislation addresses the need for clarity and distinguishing between compounding by a pharmacy and the activities of a compounding outsourcer. It assigns responsibility and accountability to the FDA for regulating compounding manufacturers while preserving the accountability for pharmacy compounding to State Boards of Pharmacy. It also establishes a user fee program to help ensure that the FDA has the resources it needs to effectively regulate compounding manufacturers.

Because of the potential nationwide scale of these operations, we are concerned that State Boards of Pharmacy may not be able to provide adequate oversight of these facilities. Many State boards may not have the resources or expertise to evaluate whether a pharmacy has crossed the line and become a manufacturer.

With respect to the regulatory framework proposed in the draft legislation by Representative Griffith, ASHP is concerned that the regulatory environment that allowed the New England Compounding Center to operate as a pharmacy would remain intact. In other words, if authority between State Boards of Pharmacy and FDA is unclear due to lack of accountability, we would be concerned that neither FDA nor State boards could be held accountable if an entity were licensed as a pharmacy, but was also preparing sterile compounded preparations without a prescription and selling across State lines.

In addition, our understanding of the draft legislation is that FDA would only be permitted to inspect a pharmacy that may be operating as a large scale compounding entity if FDA has received a submission from the State Board of Pharmacy.

This ability for FDA to have the necessary access to records and inspect a compounding entity would be contingent upon State boards being properly equipped with trained personnel to determine if an activity appears to approach manufacturing. We are concerned that FDA may not be fully accountable if the State board does not notify the agency.

Further, this approach would imply that State boards would inspect all prescription records and sales transactions of each licensed pharmacy in their State to identify those entities that may be acting outside the scope of traditional pharmacy compounding. Therefore, it would be referred to the FDA. We do not see that as realistic for many State boards, and therefore believe that these types of compounding outsourcers would be more appropriately regulated by FDA.

In conclusion, ASHP remains completely committed to working with Congress, the FDA and other stakeholders in developing a reformed regulatory framework for pharmacy compounding. Thank you, Chairman Pitts, for holding this hearing on this very important public health topic.

Mr. PITTS. The chair thanks the gentleman.

[The prepared statement of Mr. Thompson follows:]

House Energy and Commerce Committee
Subcommittee on Health

Hearing on

Reforming the Drug Compounding Regulatory
Framework

July 16, 2013

Oral Statement for the Record
Submitted by the



American Society of Health-System Pharmacists

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Good afternoon and thank you Chairman Pitts and Ranking Member Pallone and distinguished Members of the Subcommittee, for holding this hearing. My name is Kasey Thompson, and I serve as Vice President of Policy, Planning and Communications at the American Society of Health-System Pharmacists (ASHP). I am here today to provide ASHP's perspective as a professional society that represents over 42,000 pharmacists who practice in hospitals, health systems, and ambulatory clinics, and has been a recognized leader for over 20 years in the development of guidelines on compounding and working with compounding outsourcers.

The event caused by the New England Compounding Center resulted in 61 unnecessary deaths and more than 700 meningitis cases. ASHP strongly believes that the authority and accountability between the FDA and state boards of pharmacy needs to be clarified. We applaud the work that Congress has done so far to address this highly complex patient safety and public policy issue, and also commend the National Association of Boards of Pharmacy for its efforts to help states gain better insights into the quality and level of compounding practices throughout the country. We are hopeful that a legislative solution that protects the public and provides assurances to health care professionals that the products they purchase from compounding entities are safe is found before the 1-year anniversary of the NECC tragedy.

We believe that compounding outsourcers that prepare customized sterile preparations that are not commercially available should be held to the highest standards for quality, including relevant Current Good Manufacturing Practices, and should be required to be registered with and routinely inspected by the FDA. Further, we believe that these entities should not copy commercially available products *except* in the case of drug shortages or to make a medically necessary variation that meets patient-specific needs. The drug approval process in the United States is the gold standard, and it should be maintained as such.

However, it is important to recognize that there are many legitimate and medically necessary compounded sterile preparations that simply are not available from a brand or generic manufacturer in the strength or dosage form that the patient needs.

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U.S. hospitals prepare a vast array of compounded sterile preparations from FDA-approved products every day in order to meet patient-specific needs. The compounded medications that hospitalized patients need range from simple intravenous admixtures to complex customized medications that are not available off the shelf, such as multi-ingredient cardioplegia solutions for heart surgery, precisely measured combinations of epidural pain medication for women in labor and delivery, concentrated pain medications for cancer patients, and adult medications prepared in concentrations that can be safely administered to babies and children.

Where necessary, hospitals enlist the services of qualified compounding outsourcers for some preparations for several reasons. For example, some hospitals may not have the necessary equipment or facilities to prepare some high-risk sterile preparations, which is sometimes the case in small and rural hospitals with limited resources. Or, they may face medication shortages for commercial products that can only be replicated by outside suppliers that provide customized compounded sterile preparations. They may also enlist the help of outsourcers to provide FDA-approved sterile products in ready-to-administer packages in the strength and dosage forms they need.

The compounding outsourcing industry that has evolved over the last decade provides critical services to hospitals, physician offices, outpatient surgery centers, and other patient-care settings. The vast majority of the products that outsourcers prepare is for anticipatory use, and does not have a prescription at the time of sale. However, it is important to note that in the hospital and health-system setting, all medications have a medication order from an authorized prescriber before the medication is administered to the patient.

The evolution of the compounding outsourcing industry has outpaced the ability of state and federal laws to keep up, creating legal and regulatory gray areas between states and the federal government. Various challenges in the courts to federal authority to regulate pharmacy compounding have also created uncertainty regarding jurisdiction. Unfortunately, it just isn't as simple as calling these large-scale anticipatory compounding entities that often engage in interstate commerce a pharmacy, repackager, or pharmaceutical manufacturer. They are something in between each of these, but no one category fits them perfectly.

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Recent bipartisan Senate legislation (S.959) appears to address the need for clarity in distinguishing between compounding by a pharmacy and the activities of a compounding outsourcer. It assigns responsibility and accountability to the FDA for regulating what S. 959 terms “compounding manufacturers” while preserving the accountability for pharmacy compounding to state boards of pharmacy. It also establishes a user fee program to help ensure that the FDA has the resources it needs to effectively regulate compounding manufacturers.

Because of the potential nationwide scale of these operations, we are concerned that state boards may not be able to provide adequate oversight of these facilities. Many state boards may not have the resources or expertise to evaluate whether a pharmacy has crossed the line and become a manufacturer.

With respect to the regulatory framework proposed in draft legislation by Representative Griffith, ASHP is concerned that the regulatory environment that allowed the New England Compounding Center to operate as a pharmacy would remain intact. In other words, if authority between state boards and FDA is unclear due to a lack of accountability, we would be concerned that neither FDA nor state boards could be held accountable if an entity were licensed as a pharmacy but was also preparing sterile compounded preparations without a prescription and selling across state lines.

In addition, our understanding of the draft legislation is that FDA would only be permitted to inspect a pharmacy that may be operating as a large-scale compounding entity if FDA has received a submission from a state board of pharmacy. This ability for the FDA to have the necessary access to records and inspect a compounding entity would be contingent on state boards being properly equipped with trained personnel to determine if an activity appears to approach manufacturing. We are concerned that FDA may not be fully accountable if the state board does not notify the agency.

Further, this approach would imply that state boards would inspect all prescription records and sales transactions of each licensed pharmacy in their state to identify those entities that may be acting outside the scope of traditional pharmacy and should therefore be referred to FDA. We do

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not see that as realistic for many states boards of pharmacy, and therefore believe that these types of compounding outsourcers would be more appropriately regulated by the FDA.

Conclusion

ASHP remains completely committed to working with Congress, the FDA, and other stakeholders in developing a reformed regulatory framework for pharmacy compounding. The end result will give patients and health care professionals the assurance that those entities compounding large-scale, non-patient-specific preparations are properly regulated and are producing safe products.

Thank you again Chairman Pitts and Ranking Member Pallone for holding this hearing on this important public health issue.

Mr. PITTS. Mr. Francer, you are recognized 5 minutes for an opening statement.

STATEMENT OF JEFFREY FRANCER

Mr. FRANCER. Thank you, Mr. Chairman and members of the subcommittee. I am Jeff Francer, I serve as assistant general counsel of the Pharmaceutical Research and Manufacturers of America. Thank you for the opportunity to present our views this afternoon.

PhRMA is a voluntary, nonprofit association that represents the country's leading pharmaceutical research and biotechnology companies. In 2012, PhRMA's members alone invested nearly \$50 billion in discovering and developing new medicines. PhRMA shares the committee's goal of advancing public health and protecting patient safety by ensuring that FDA's statutory authority and safety standards for pharmacy compounding are strong enough to protect patients against the risks demonstrated over the past year.

There is no higher priority for biopharmaceutical companies than patient safety. We commend the committee's diligence in investigating the causes of the recent tragedies and examining potential solutions.

PhRMA believes that medicines manufactured by our member companies as well as those manufactured by nontraditional pharmacies and manufacturers should be regulated by FDA using a consistent, risk-based approach. This approach best serves public health because products that present similar risks should be regulated in a similar manner.

In light of the incidents surrounding the New England Compounding Center, it is clearly appropriate for Congress to revisit the FDA's authority to regulate compounding of prescription drugs. And consistent with the goals of clarifying FDA's authority and protecting patient safety, PhRMA would support legislation that would include the following seven attributes:

First, clarify that FDA retains its strong existing authority to regulate as a new drug any medicine that is compounded outside of traditional compounding. Large-scale, commercial manufacturing of prescription medicine should be governed by the same high standards, whether the commercial producer is designated as a pharmacy or as a manufacturer.

Second, the legislation would provide express inspection and registration authority for nontraditional compounders as manufacturers, including to the extent that such authority is not clear the ability to inspect records to determine whether pharmacies are actually engaging in nontraditional compounding.

Third, provide user fee authority which we believe already exists, to ensure that FDA has adequate resources to regulate nontraditional compounders as manufacturers.

Fourth, ensure that nontraditional compounders may not compound copies of marketed drugs and thus subvert FDA's generic and bio similar approval processes.

Fifth, prohibit the compounding of specific drugs or drug categories for safety reasons.

Sixth, appropriately limit the channels of distribution of compounded drugs, including through a prohibition on wholesale distribution.

And finally, any new legislation should resolve any ambiguity in FDA's current authority by deleting the section of the Federal Food, Drug, and Cosmetic Act at issue in the *Western States* case.

Within this framework, FDA could and should take a risk-based approach to the regulation of nontraditional compounding using the same approach that FDA now takes to pharmaceutical manufacturing. However, complex legislation that creates a whole new classification of compounder, so-called compounding manufacturers, is unnecessary. Such an approach could result in regulatory confusion and the application of different regulatory standards for similar types of manufacturing. In fact, such a third class would actually decrease FDA's current statutory standards for regulating non-traditional compounders.

Finally, PhRMA is concerned about risks to patient safety that could result from proposals to allow compounding of copies of marketed pharmaceuticals in the event of a drug shortage. This potential exception could expose patients to unsafe drugs because the compounder need not establish that the compounded version has a safety and efficacy profile equivalent to the FDA-approved product.

In conclusion, Mr. Chairman, PhRMA thanks the subcommittee for the opportunity to provide testimony this afternoon regarding how to clarify FDA's existing authority to regulate nontraditional compounding. Biopharmaceutical companies are committed to patient safety. The same safety standards that govern pharmaceutical manufacturing should also protect patients who are treated with medicines manufactured by large-scale compounders. And we look forward to continuing the work with the subcommittee as it continues this important task.

Mr. PITTS. The chair thanks the gentleman.

[The prepared statement of Mr. Francer follows:]



Statement of
Jeffrey K. Francer
Assistant General Counsel
Pharmaceutical Research and Manufacturers of America

Before the
Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives

"Reforming the Drug Compounding Regulatory Framework"

July 16, 2013

Statement of the Pharmaceutical Research and Manufacturers of America
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Mr. Chairman and members of the Subcommittee, I am Jeffrey Francer, and I serve as Assistant General Counsel of the Pharmaceutical Research and Manufacturers of America (PhRMA). Thank you for the opportunity to present our views on improving the drug compounding regulatory framework in order to enhance patient safety.

PhRMA is a voluntary, nonprofit association that represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. In 2012, PhRMA members alone invested nearly \$50 billion in discovering and developing new medicines.

PhRMA shares the Committee's goal of advancing public health by ensuring that the Food and Drug Administration's (FDA) statutory authority and safety standards for pharmacy compounding are adequate to protect patients against the risks demonstrated over the past year.

There is no higher priority for biopharmaceutical companies than patient safety. We commend the Committee's diligence in investigating the causes of the recent tragedies involving pharmacy compounding and potential solutions.

PhRMA believes that medicines manufactured by our member companies, as well as those compounded by non-traditional pharmacies and manufacturers, should be regulated by FDA using a consistent, risk-based approach. This approach best serves the public health, because products that present similar risks should be regulated similarly.

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PhRMA Supports FDA Oversight of Non-traditionally Compounded Drugs to Patients

In light of the incidents surrounding the New England Compounding Center (NECC) last year, it is clearly appropriate for Congress to revisit FDA's authority and obligations with respect to the compounding of prescription drugs. The ultimate objective of this endeavor should be, first and foremost, to ensure the safety of patients.

After reviewing FDA's existing enforcement authority, including the authority FDA applied to inspect NECC prior to the tragedy, PhRMA believes that patient health could be better protected by (1) clarifying FDA's existing authority to regulate non-traditional compounding, to the extent there is any ambiguity, and (2) ensuring that FDA has sufficient resources to protect the public health, including by considering its current authority to levy user fees on manufacturers to bolster its inspection resources.

Consistent with the goal of clarifying FDA's authority to regulate non-traditional compounding and ensuring that the agency has the resources necessary to protect public health, PhRMA would support legislation that would:

1. Clarify that FDA retains authority to regulate as a new drug (including through the application requirement and adulteration and misbranding provisions) any drug that is compounded outside of traditional compounding (*i.e.*, non-individual compounding), and any person involved in the manufacture, distribution, or marketing of such drugs;
2. Provide express inspection and registration authority for non-traditional compounders as manufacturers, including, to the extent that such authority is not clear, the ability to inspect records to determine whether pharmacies are engaging in non-traditional compounding;

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3. Provide specific user fee authority to ensure that FDA has adequate resources to regulate non-traditional compounders as manufacturers;
4. Ensure that non-traditional compounders may not compound copies of marketed drugs subject to a new drug application (NDA) or biologics license application (BLA), including slight variations of those marketed drugs that are not intended for specific individuals for whom the variation is clinically important, and thus subvert the generic or biosimilar approval process;
5. Prohibit the compounding of specific drugs or drug categories, whether by statute or by giving the agency the discretion to exclude them on safety or efficacy grounds (*e.g.*, complex dosage forms and biologics, drugs removed from the market for reasons of safety or efficacy, and products containing drug substances that FDA has determined may not be used in compounding);
6. Appropriately limit the channels of distribution for compounded drugs, including through a prohibition on wholesale distribution; and
7. Delete the section of the Federal Food, Drug, and Cosmetic Act (FDCA) at issue in *Thompson v. Western States Medical Center*, section 503A(c).¹

Within this framework, FDA could and should take a risk-based approach to the regulation of non-traditional compounding and prioritize inspections and enforcement using the same risk-based approach the agency applies to pharmaceutical manufacturing.

¹ 535 U.S. 357 (2002).

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Comprehensive and complex legislation that creates a new classification of compounder (so-called "compounding manufacturers") is, however, unnecessary. Such an approach could result in regulatory confusion (both federal and state) and the application of different regulatory standards (and patient protections) for similar types of manufacturing. PhRMA does not believe that the creation of a new class of non-traditional compounding subject to standards different than NDA- or BLA-approved drugs and biologics best serves the public health. In fact, such a "third class" would actually decrease FDA's current statutory standards for regulating non-traditional compounders.

PhRMA Supports FDA's Use of its Existing Authority to Regulate Compounded Drugs and Biologics

A. Background on the Regulation of Biopharmaceutical Manufacturers

As mentioned at the outset, patient safety is the highest priority for PhRMA and biopharmaceutical companies that research, develop, manufacture, and bring to market new medicines. Biopharmaceutical research companies develop and market prescription medicines in accordance with FDA's exacting regulatory standards and industry practices. Our companies typically invest over \$1.2 billion and 10 to 15 years to bring each new medicine to market. This investment includes performing nonclinical tests and extensive clinical trials to demonstrate safety and effectiveness, submission of an NDA or BLA for review and approval by FDA, establishing systems to assure manufacturing quality, and maintaining pharmacovigilance systems and other measures

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to identify and respond to safety issues that may arise after pharmaceutical products are made available for use by patients.

In addition to complying with the requirement to obtain FDA approval before a new drug may be sold in the United States, biopharmaceutical research companies comply with the “gold standard” of quality manufacturing: FDA’s current Good Manufacturing Practice (cGMP) regulations.² These regulations apply to all new prescription drugs approved for sale in the United States, wherever they are made, and extend to all components of a finished drug product, including active pharmaceutical ingredients, wherever they are sourced. FDA’s cGMP requirements are based on the fundamental quality assurance principle that quality, safety, and effectiveness “cannot be inspected or tested into a finished product,” but instead must be designed and built into a product.³

It is well established that inspections alone cannot be relied upon to ensure product quality and integrity, and that quality systems are vital to ensuring each product meets established specifications and requirements.⁴ The quality systems approach to manufacturing drug products is embodied in the cGMP regulations and embraced by biopharmaceutical companies throughout the manufacturing process.

As the Subcommittee discussed during its last hearing on this topic, the FDCA requires that manufacturers provide proof of their ability to maintain a quality system, including the ability to manufacture under cGMP conditions, as part of the new drug

² Under current law, a drug is adulterated if the methods used in, or the facilities or controls used for, manufacturing a drug product do not conform to cGMP. 21 U.S.C. § 351(a)(2)(B). FDA regulations and guidance provide additional clarification regarding the expectations of cGMP in drug product manufacturing.

³ 61 Fed. Reg. 20104, 20105 (May 3, 1996).

⁴ See generally 21 C.F.R. Parts 210 and 211.

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application. FDA also requires a pre-approval facility inspection for pharmaceutical manufacturers. In order to ensure patient safety, the agency should apply these same standards to non-traditional compounders that perform manufacturing steps and whom are regarded manufacturers under the FDA.

B. FDA Has the Authority to Regulate Non-traditionally Compounded Drugs and Biologics

PhRMA fully supports thorough FDA oversight of all compounded drugs and biologics manufactured outside of the exception for traditional pharmacy compounding under section 503A of the FDCA. The manufacturing of medicines, whether by manufacturers or pharmacies, should be regulated in a consistent, risk-based manner. The touchstone of such an approach is ensuring both safety and efficacy for patients.

Large-scale, commercial manufacturing of prescription medicines (including non-traditional compounding) should be governed by the same high standards as biopharmaceutical manufacturing—whether the producer is designated as a “pharmacy” or as a “manufacturer.” At an absolute minimum, entities that engage in large-scale commercial production of pharmaceutical compounding should be subject—and in our view are currently subject—to the same cGMP requirements for quality manufacturing as are pharmaceutical manufacturers, with clear provision for inspections and enforcement actions by FDA. Moreover, large-scale compounding without a valid NDA or BLA would render the products unapproved new drugs in violation of section 505 of the FDCA.

It is our understanding that section 503A of the FDCA, as passed in 1997, was intended to accomplish these objectives. In other words, Congress intended for large-scale, commercial production of medicines to be regulated by FDA applying cGMP

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standards. PhRMA supports this goal. Despite some uncertainty as to the enforceability of 503A due to a disagreement between two federal courts of appeal concerning the severability of the advertising restrictions in section 503A(c) that were invalidated by the Supreme Court in *Western States*,⁵ PhRMA believes FDA has ample authority to regulate large-scale compounders under the other provisions of 503A and the general provisions of the FDCA.

FDA itself has taken this position in a Compliance Policy Guide (CPG) that it issued following the *Western States* decision. The CPG assumed that section 503A was invalid but nevertheless asserted the agency's authority to regulate large-scale, commercial compounding operations.⁶ At that time, the agency stated, "[w]hen the scope and nature of a pharmacy's activities raise the kinds of concerns normally associated with a drug manufacturer and result in significant violations of the new drug, adulteration, or misbranding provisions of the Act, FDA has determined that it should seriously consider enforcement action."⁷ FDA's compliance guidance also contains other criteria to help determine whether purported compounders should be subject to FDA's cGMP manufacturing requirements. These criteria include:

- Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions.
- Compounding finished drugs from bulk active ingredients that are not components of FDA approved drugs without an FDA sanctioned investigational

⁵ 535 U.S. 357 (2002).

⁶ FDA, Compliance Policy Guide Section 460.200 (May 29, 2002).

⁷ *Id.*

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new drug application (IND) in accordance with 21 U.S.C. § 355(i) and 21 C.F.R. 312.

- Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA-registered facility.
- Using commercial scale manufacturing or testing equipment for compounding drug products.
- Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.
- Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products. In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA-approved drug that is commercially available. In these circumstances, FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient.

As the Committee's investigation has revealed, FDA had actually exercised some of its available enforcement authority in connection with the NECC compounding situation. For example, FDA carried out inspections of compounding pharmacies, worked with state authorities to suspend operations in noncompliant facilities, and arranged for recalls of potentially violative products.

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To the extent that it may help clarify FDA's regulatory authority, PhRMA supports the amendment of section 503A to delete the promotional provisions in 503A(c) as well as to confirm the agency's authority to regulate compounded drugs under the remaining provisions of section 503A. PhRMA also would support legislation that expressly provides FDA with inspection and registration authority for non-traditional compounds as manufacturers of new drugs and provides for user fees to ensure that FDA has adequate resources to regulate such compounds.

The Creation of a New Regulatory Class—the “Compounding Manufacturer”—Unnecessarily Complicates the Existing Regulatory Scheme and Threatens Patient Safety

Consistent with FDA's compliance guidance, PhRMA believes that, with the exception of drugs and biologics compounded by state-licensed pharmacists (or state-licensed physicians) upon receipt of a prescription for an identified individual patient or in limited quantities based on a history of prescription orders, compounded drugs and biologics are unapproved new drugs or unlicensed biologics subject to FDA regulation under the FDCA and Public Health Service Act (PHSA). These drugs and biologics therefore require regulatory approval through an NDA, abbreviated NDA, or BLA. Drug products distributed in interstate commerce without an NDA would also be misbranded in violation of the FDCA.

The public health is best served when FDA regulates medical treatments consistent with the risks they present. Medicines that present similar risks should be regulated similarly. Accordingly, PhRMA believes large-scale compounding entities that are engaged in the manufacturing of compounded drugs and biologics (which would

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include "compounding manufacturers," as defined in the Senate bill) should be regulated in the same manner as traditional biopharmaceutical manufacturers.

PhRMA is, however, deeply concerned that the creation of a new "compounding manufacturer" classification will upset FDA's longstanding regulatory distinction between the activities of federally regulated manufacturers, on the one hand, and the activities of state-regulated pharmacists, on the other hand. Exempting "compounding manufacturers" from the requirement to obtain an approved NDA or BLA raises patient safety concerns; indeed the application requirement is critical for proving to FDA that the manufacturer is able to create large batches of drug products safely and consistently. In addition, the complexities and myriad exceptions associated with the Senate bill's proposed "compounding manufacturer" category may result in further confusion and an inconsistent regulatory scheme.

Establishing a new third class of compounder would create an overly complex and confusing manner that could be difficult to implement. For example, it is unclear how a large-scale sterile product compounder would be treated differently if it stopped compounding sterile products but continued manufacturing large batches of non-sterile medicines. Significant FDA and state resources may be required to resolve open questions about the scheme. These resources would better protect the public health if used for inspections and enforcement under FDA's existing authority over non-individual compounders.

Accordingly, PhRMA supports clarification of FDA's existing authority to apply a risk-based approach to the oversight of non-traditional compounding and not a new patchwork that would create a new sub-class of non-individual compounders.

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Finally, PhRMA is concerned about risks to patient safety that could result from proposals to allow pharmacy compounding of “copies” of marketed pharmaceuticals in the event of a drug shortage. This potential exception could expose patients to unsafe drugs, because the compounder need not establish that the compounded version has a safety and efficacy profile equivalent to the FDA-approved product.

Commercial drug shortages may result from factors such as a manufacturer’s determination that particular ingredients fail to meet the manufacturer’s quality standards, or due to the implementation of new manufacturing processes designed to produce more finished products that meet FDA-approved release specifications. Compounding manufacturers may be using the same ingredients or methods a biopharmaceutical manufacturer (or FDA) deemed insufficient. Moreover, sponsors’ efforts to coordinate closely with FDA’s drug shortages group to address a shortage could be confounded by this alternative supply.

Conclusion

PhRMA thanks the Committee for the opportunity to provide testimony regarding how to clarify FDA’s authority to regulate non-traditional compounding. Biopharmaceutical companies are committed to patient safety. The same safety standards that govern biopharmaceutical manufacturing should also protect patients who are treated with medicines manufactured by large-scale compounders. PhRMA would support legislation clarifying the agency’s ability to regulate non-traditional compounders, however we believe that an entirely new regulatory scheme is unnecessary to correct the enforcement issues surrounding the tragic NECC incident.

Mr. PITTS. Dr. Gaugh, you are recognized for 5 minutes for opening statement.

STATEMENT OF DAVID GAUGH

Mr. GAUGH. Thank you, Chairman Pitts and members of the House Energy Subcommittee on Health, and thank you for inviting me to testify before the subcommittee on this very important topic of drug compounding.

My name is David Gaugh. I am senior vice president for Sciences and Regulatory Affairs at the Generic Pharmaceutical Association and a licensed pharmacist.

GPhA represents the manufacturers and distributors of finished dose generic pharmaceuticals, bulk pharmaceuticals and suppliers of other goods and services to the generic industry.

The quality and affordability of generic medicines is vital to the public health and sustainability to the health care system. Prior to joining GPhA, I was general manager of a generic injectable manufacturing company. I also served a leadership role in a major group purchasing organization and was assistant director of pharmacy in a hospital system in the Midwest where one of my responsibilities was oversight of traditional compounding performed by my staff.

GPhA supports the goal of clarifying the FDA's authority over compounding in order to protect patient safety and prevent another health care crisis like the fungal meningitis outbreak that was caused by the substandard compounded drugs.

Traditional compounding plays a vital role for patients and any new regulation should maintain that role. GPhA firmly believes that pharmacy compounding should adhere to the standard of one patient, one prescription, one drug. Patient safety is the highest priority for approved pharmaceutical manufacturers who comply with quality and sterile manufacturing processes and procedures as defined by the current good manufacturing practices, or cGMP. These regulations and associated guidances apply to all prescription drugs approved by the FDA for sale in the U.S.

The FDA's regulations and guidance are based on the fundamental principles that quality cannot be inspected or tested into a finished product, but quality must be designed into the product and the manufacturing process.

The large-scale manufacturing of sterile medicines, no matter who performs the functions, must involve similar activities as they have similar potential risks. In order to ensure the safety of the American public, the large-scale manufacturer of these sterile medicines should be regulated by the FDA in a consistent risk-based manner at the same high standards, including submitting documentation to the FDA and submitting to both preapproval and routine risk-based cGMP inspections.

A sterile injectable drug should not be the object of compounding unless these aforementioned regulations and guidances are enforced by the FDA or if the product is compounded for an individual patient by an individual prescriber.

GPhA strongly supports established standards for the quality of bulk substances used in compounding. We believe it is critical that these standards should include a requirement to the bulk substance used in compounding be from FDA inspected cGMP-compli-

ant facilities, and that should be done prior to the compounding. GPhA recognizes that many in Congress believe that there should be an exemption to these requirements for certain medically necessary sterile products and shortage. We believe that the requirements for any category of large-scale compounding of sterile products should be the same FDA standards that apply to pharmaceutical manufacturers.

To solve a drug shortage of sterile injectable marketed drugs by lowering oversight, safety and quality standards is not in the best interests of the American public.

GPhA believes any drug substance exemption should include explicit language clarifying that the large scale compounder that is compounding marketable products on the FDA drug shortage list must immediately stop both the compounding and the distribution once notified by the FDA through established processes that the shortage has ended.

GPhA strongly supports the requirement for large scale compounding pharmacies or compounding manufacturers that plan to compound a marketed drug on the official FDA drug shortage list notify the FDA prior to starting that compounding.

We do not believe it is appropriate for notification only after initial large scale compounding has started. Additionally, the FDA should be given the authority to deny the request for compounding of a drug on the drug shortage list.

GPhA strongly supports providing the FDA with the additional resources needed to conduct inspections and do effective oversight through the fees on large-scale compounders. These fees should be sufficient to ensure that resources are not diverted from other areas within the agency.

In the interest of providing health care professionals and patients with complete information, any product compounded outside of the institution in which it is administered should be appropriately labeled as determined by the FDA and identified as a compounded product.

GPhA believes large-scale compounding pharmacies should be held to same adverse events reporting requirements as pharmaceutical manufacturers to allow the FDA ability to earlier identify and prevent any future health crisis.

In conclusion, Mr. Chairman, GPhA and our member companies are committed to ensuring both the role of the traditional compounders for patients, that need these patients are used and are safe for the patients and we look forward to working with the committee on this very important factor. Thank you.

Mr. PITTS. The chair thanks the gentleman.

[The prepared statement of Mr. Gaugh follows:]



SUMMARY OF TESTIMONY OF DAVID GAUGH

SENIOR VICE PRESIDENT FOR SCIENCES AND REGULATORY AFFAIRS, GENERIC PHARMACEUTICAL ASSOCIATION

“REFORMING THE DRUG COMPOUNDING REGULATORY FRAMEWORK”

BEFORE THE ENERGY AND COMMERCE SUBCOMMITTEE ON HEALTH, U.S. HOUSE OF REPRESENTATIVES
JULY 16, 2013

Patient Safety: GPhA supports the goal of clarifying FDA’s authority over compounding in order to protect patient safety and prevent another public health crisis.

Traditional Compounding: Traditional compounding plays a vital role for patients, and any new regulation should maintain that role. Pharmacy compounding should adhere to the standard of “one patient, one prescription, one drug.”

Good Manufacturing Practices - Sterile Products: The FDA’s regulations for pharmaceutical manufacturers are based on the principle that quality cannot be inspected or tested into a finished product, but quality must be designed into the product and manufacturing processes. cGMP regulations establish the regulatory framework in the U.S. as the blueprint for assuring safety and efficacy. The large-scale manufacture of sterile medicines – no matter who performs this function – must involve similar activities as they have similar potential for risk, and should therefore be regulated in a consistent, risk-based manner. All large-scale manufacturers of sterile injectable medicines should be required to prove that they can manufacture these medicines consistently and safely, through documentation to the FDA and submitting to both preapproval and routine risk-based cGMP inspections. A sterile injectable drug should not be the object of compounding, unless these aforementioned regulations and guidances are enforceable by the FDA or if the products are compounded for a specific individual patient, per a physician prescription.

Bulk Drug Substances: GPhA strongly supports establishing standards for the quality of the bulk substances used in compounding.

Drug Shortage Exemption: To solve a drug shortage by lowering safety and quality standards is not in the best interest of the public health. Any drug shortages exemption should also clarify that sterile products on the drug shortage list cannot be compounded indefinitely.

Notification Prior to Compounding: GPhA strongly supports a requirement for large-scale compounding pharmacies and “compounding manufacturers” who plan to compound a marketed drug on the shortage list to notify FDA prior to the start of compounding.

Pre-marketing Registration, Inspections & Fees: GPhA believes that large-scale compounders and “compounding manufacturers” should be subject to pre-marketing inspections by FDA, and FDA should be provided with the resources needed through fees on these large-scale compounders or “compounding manufacturers.”

Labeling: In the interest of providing physicians and patients with complete information, any product compounded outside of the institution in which it will be administered should be labeled as a compounded product.

Adverse Event Reporting: Large-scale compounding pharmacies and “compounding manufacturers” should be required to report adverse events to FDA.



TESTIMONY OF DAVID GAUGH

SENIOR VICE PRESIDENT FOR SCIENCES AND REGULATORY AFFAIRS

GENERIC PHARMACEUTICAL ASSOCIATION

**"REFORMING THE DRUG COMPOUNDING REGULATORY
FRAMEWORK"**

BEFORE THE ENERGY AND COMMERCE SUBCOMMITTEE ON HEALTH

UNITED STATES HOUSE OF REPRESENTATIVES

JULY 16, 2013

Good afternoon Chairman Pitts, Ranking Member Pallone, and Members of the House Energy and Commerce Subcommittee on Health. Thank you for inviting me to testify before the Subcommittee on the important topic of drug compounding.

I am David Gaugh, Senior Vice President for Sciences and Regulatory Affairs at the Generic Pharmaceutical Association (GPhA) and a licensed pharmacist. GPhA represents the manufacturers and distributors of finished dose generic pharmaceuticals, bulk pharmaceuticals, and suppliers of other goods and services to the generic industry. Generic pharmaceuticals now fill 84 percent of all prescriptions dispensed in the United States but account for only 27 percent of the total spending for prescription medicines. According to an analysis by IMS Health, the world's leading data source for pharmaceutical sales, the use of FDA-approved generic drugs has saved U.S. consumers, patients and the health care system more than \$1 trillion over the past decade — which equates to \$1 billion in savings every other day. The quality and affordability of generic medicines is vital to public health and the sustainability of the health care system.

Prior to joining GPhA, I was Vice President and General Manager for Bedford Laboratories, the generic injectable division of Ben Venue Laboratories and a wholly owned subsidiary of Boehringer Ingelheim. I have also served as Senior Director, Pharmacy Contracting and Marketing, for VHA/Novation, one of the largest Group Purchasing Organizations in the U.S., and was System Director of Pharmacy for a

regional referral tertiary-care healthcare system in the Midwest, where one of my responsibilities was the oversight of traditional compounding performed by my staff.

Patient Safety

GPhA supports the goal of clarifying the FDA's authority over compounding in order to protect patient safety and prevent another public health crisis like the fungal meningitis outbreak caused by substandard and contaminated compounded drugs from the New England Compounding Center (NECC). I appreciate the opportunity to outline GPhA's principles on appropriate regulation of pharmaceutical compounding in order to prevent substandard products from reaching patients.

Traditional Compounding

Traditional compounding plays a vital role for patients, and any new regulation should maintain that role. GPhA firmly believes that pharmacy compounding should adhere to the standard of "one patient, one prescription, one drug." In other words, a pharmacist or compounding pharmacy should engage in compounding in response to a single prescription, written for a single patient, and the patient should receive the prescribed finished product (drug).

A national, uniform set of requirements for compounding is needed to ensure that all patients receive safe compounded drugs. We support clarifying that compounded drugs are subject to the Federal Food, Drug, and Cosmetic Act.

GPhA supports a federal requirement for compounding pharmacies to comply with USP standards for sterile pharmaceutical compounding. More specifically, GPhA supports USP 797, a longstanding practice in sterile pharmaceutical preparation, as a minimum Federal and/or State standard. We believe that all compounding pharmacies and other practitioners who compound sterile preparations, and the sterile products they compound, should fall under this standard.

Additionally, there are certain complex, high-risk products for which patient safety concerns preclude compounding under any circumstances.

Good Manufacturing Practices – Sterile Products

Patient safety is the highest priority for approved pharmaceutical manufacturers. These companies comply with quality and sterile manufacturing processes and procedures as defined by the FDA's current Good Manufacturing Practice (cGMP) regulations and associated guidance documents. These regulations and guidance documents apply to all prescription drugs approved by the FDA for sale in the United States, no matter what country they are manufactured in, and extend to all ingredients (active and inactive) and components of a finished drug product. The FDA's regulations and guidances are based on the fundamental principle that quality cannot be inspected or tested into a finished product, but quality must be designed into the product and manufacturing processes. These regulations and guidances also drive manufacturers to establish a quality systems approach to assuring consistent quality.

In pharmaceutical manufacturing, quality systems and cGMP requirements begin at the product development stage. The FDA requires that a drug application – a New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) – describe the quality safeguards for the proposed manufacturer of the product in the application. Part of the evidence required by the FDA to demonstrate safety and effectiveness is the requirement that a manufacturer provide a full description of the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of a drug. As such, ALL manufacturers must be held to these same standards.

The importance of the cGMP regulations is that they establish the regulatory framework in the U.S. as the blueprint for assuring safety and efficacy. Whether you are a small start-up manufacturer or a large multinational manufacturer, the regulations and guidance documents provide the single template for success. From the construction of facilities, to selection of equipment, to training of employees, to designing quality into a manufacturing process, to the selection of materials and suppliers, to the final approval to distribute product, the regulations and guidelines provided by the FDA are the foundation for a consistent risk-based approach to assure quality.

The large-scale manufacture of sterile medicines – no matter who performs this function – must involve similar activities as they have similar potential for risk. These large-scale sterile manufacturing functions involve the mixing of active and inactive ingredients, the finish fill of the product and the packaging of the product. Therefore, in order to assure the safety of the American public, the large-scale manufacture of these sterile

medicines, whether by pharmaceutical manufacturers or compounding pharmacies, should be regulated in a consistent, risk-based manner. As such, consideration for large-scale commercial manufacturing of prescription medicines, whether the producer is designated as a "compounding manufacturer" or as a pharmaceutical manufacturer, must be governed by the same high standards as pharmaceutical manufacturing are held to today. Thereby, all must be held to the same inspection and enforcement actions by the FDA. As such, all large-scale manufacturers of sterile injectable medicines should be required to prove that they can manufacture these medicines consistently and safely by submitting documentation to the FDA and submitting to both preapproval and routine risk-based cGMP inspections.

Based on the framework I have just provided, any large-scale manufacturer of sterile injectable medicines should comply with these same regulations and guidances. A large-scale manufacturer, which is in full compliance, will have a high degree of assurance that the medicines they produce will be of consistently high quality and sterility. A large-scale company making thousands of doses of medicines, whether labeled a "compounding manufacturer" or a pharmaceutical manufacturer should be regulated in a similar manner when it performs similar manufacturing steps and presents similar risks to patients. Therefore, a sterile injectable drug should not be the object of compounding, unless these aforementioned regulations and guidances are enforceable by the FDA or if the products are compounded for a specific individual patient, per a physician prescription, and adhering to the standard of "one patient, one prescription, one drug."

Bulk Drug Substances

GPhA strongly supports provisions establishing standards for the quality of the bulk substances used in traditional or large-scale compounding. We believe that these standards should also include a requirement that the bulk substances used in compounding be from FDA-inspected, cGMP compliant facilities.

The FDA should inspect and approve bulk substances manufacturing facilities *prior to* the initiation of any compounding activities. A requirement for compounding pharmacies or “compounding manufacturers” to only use bulk substances manufactured by facilities registered with the FDA is an important step in ensuring the quality of the bulk substances used in compounding. The registration requirement itself, however, does not necessarily guarantee a facility has been inspected by the FDA – the inspection requirement for a bulk substances facility is triggered by the New Drug Application (NDA) or Abbreviated New Drug Application (ANDA), not by the filing of a Drug Master File (DMF) for the bulk substances facility. Because compounded drugs do not have an NDA or ANDA, a bulk substances facility could be registered with the FDA but not have been inspected. It is important to note that over 80% of bulk materials come from facilities outside the U.S., and the average inspection cycle of the FDA for these facilities is greater than seven years. Therefore, we believe that an additional requirement for the FDA review and approval of bulk substances facilities *prior to* compounding is critical to ensure patient safety.

Drug Shortage Exemption

GPhA recognizes that many in Congress believe that there should be an exception to these requirements for certain medically necessary, sterile products that are in drug shortage.

The generic pharmaceutical industry is committed to working with the FDA and all stakeholders to minimize current shortages and mitigate factors that could contribute to future shortages. While drug shortages represent a complex, multi-faceted issue, we are acutely aware of the distress caused to patients, families and clinicians by the shortage of critical drugs, and our industry has and will continue to work tirelessly to be part of the solution. Nothing is more important to our industry than ensuring patients have access to their lifesaving generic medications.

We believe that the requirements for any new category of large-scale compounding ("compounding manufacturers") should be the same FDA standards that apply to pharmaceutical manufacturers. To solve a drug shortage by lowering safety and quality standards is not in the best interest of the public health. Allowing large-scale compounding of sterile injectable marketed drugs, because they are in drug shortage, with less oversight and regulation than applies to pharmaceutical manufacturers, would undermine the level of safety and quality the FDA requires of current pharmaceutical manufacturers in order to protect the American public.

Applying the same quality and safety requirements that apply to FDA-approved drug manufacturers to large-scale compounders who are currently manufacturing or planning to manufacture the drugs on the drug shortage list would strengthen FDA's ability to protect patient safety. We believe that these quality and safety requirements would prevent bad actors from abusing a new category of "compounding manufacturer" to the detriment of patient safety.

GPhA believes any drug shortages exemption should include explicit language clarifying that a large-scale compounding pharmacy or "compounding manufacturer", which is compounding marketed products due to the product's inclusion on the FDA drug shortage list, cannot compound these products indefinitely. The compounder must immediately stop *both* the compounding and the distribution of these products when the shortage has ended. The FDA should also establish a process to notify the large-scale compounding pharmacies or "compounding manufacturers" of the end of the drug shortage.

We also believe that any drug shortage exemption included in legislation should be restricted to the FDA drug shortage list established under Sec. 506E of FFDCA and posted on the FDA website (www.fda.gov). We do not believe that it should also include regional shortages or private drug shortage lists.

Notification Prior to Compounding

GPhA strongly supports a requirement for large-scale compounding pharmacies or “compounding manufacturers” that plan to compound a marketed drug on the shortage list notify the FDA prior to the start of compounding. We do not believe it is appropriate for large-scale compounders to notify the FDA only after initiating large-scale compounding. Additionally, the FDA should be given the authority to deny the request of a large-scale compounding pharmacy or “compounding manufacturer” to compound a marketed drug on the shortage list, if the FDA believes it is not in the best interest of the public based on prior risk or other risk factors as identified by the Agency.

Pre-marketing Registration, Inspections & Fees

GPhA believes the registration process should also include a requirement for a large-scale compounder or “compounding manufacturer” to notify, and regularly update, the FDA of any sterile products on the shortage list it plans to compound from bulk materials.

We strongly support providing the FDA with the additional resources needed to conduct inspections through fees on large-scale compounders or “compounding manufacturers.” These fees should be sufficient for the FDA to conduct effective oversight and to ensure that resources are not diverted from other areas within the Agency.

Labeling

In the interest of providing physicians and patients with complete information, any product compounded outside of the institution in which it will be administered should be appropriately labeled as determined by the FDA and should specifically be identified as a compounded product. Additionally, any admixture/parenteral nutrition product, made with compounded sterile products, should be labeled to the patient level that compounded drugs were used in the formulation of the admixture.

Adverse Event Reporting

GPhA believes a requirement for large-scale compounding pharmacies or "compounding manufacturers" to report adverse events related to compounded products would enhance the FDA's ability to earlier identify and prevent future health crises. Large-scale compounding pharmacies or "compounding manufacturers" should be held to the same adverse event reporting requirements as pharmaceutical manufacturers.

Conclusion

In conclusion, Mr. Chairman, GPhA and our member companies are committed to ensuring both the role of traditional compounding for patients and that the products used by patients are safe. We look forward to continuing to work with this Committee and others as they develop this important legislation. Thank you, and I would be happy to answer any questions you may have.

Mr. PITTS. Mr. Coukell, you are recognized for 5 minutes for an opening statement.

STATEMENT OF ALLAN COUKELL

Mr. COUKELL. Chairman Pitts and members of the subcommittee, thank you for the opportunity to testify on pharmacy compounding and the need for legislation to protect patients.

My name is Allan Coukell. I am a pharmacist and director of drug and medical device work at the Pew Charitable Trust, independent research and policy organization with a longstanding focus on drug quality issues.

This subcommittee has heard previously about the risks of substandard compounded medicines and I won't reiterate those today, except to say that the recent fungal meningitis outbreak was far from an isolated incident, and even now, FDA inspections reveal alarming ongoing quality problems.

Today, I would like to propose ways for Congress to reduce these risks, and at the same time, ensure that patients have access to the medicines they need. Current law is inadequate for this purpose both because the courts have created uncertainty about the status of section 503A of the FDCA and because 503A does not recognize the emergence of a large scale compounding industry that is far removed from traditional pharmacy practice.

So let me begin with two points that I think all stakeholders should endorse. First, patients, doctors and pharmacists should prefer FDA-approved drugs over compounded medicines whenever possible. Only FDA-approved drugs have demonstrated their safety, efficacy and bioequivalence and have preapproved manufacturing facilities and methods. New legislation must not encourage compounding at the expense of traditional manufacturing.

Second, the preparation of customized medicines in response to a prescription for an individual patient is an established part of State-regulated pharmacy practice. But now let me make a third point, which is that there is a large-scale compounding sector that fits neither of the above categories. Instead, it does batch production of products, often high risk sterile products and admixtures of FDA-approved drugs for use in hospitals and clinics.

And the Inspector General recently reported that 85 percent of hospitals, hospitals of all sizes, large and small, purchased some intravenous drugs from outside pharmacies, sometimes thousands of doses a day. Together with the American Hospital Association and ASHP, Pew recently convened a pharmacy sterile compounding summit that brought together hospitals, purchasing organizations, compounders, regulators and pharmacy associations.

It also included experts on pharmacy and manufacturing who emphasized the enormous differences between the standards developed for pharmacy practice and the good manufacturing practices that apply to manufacturing. These experts stressed that only GMPs are adequate to ensure the safety of large scale, standardized production.

Oversight of such standards is a role for the FDA and not for State boards of pharmacy. Section 503A already recognizes FDA's responsibility to oversee some compounding, but merely reinstating the section would leave a lack of clarity about which facilities were

subject to FDA oversight, and it would not clearly give FDA the ability to ensure that large-scale compounders comply with applicable GMPs. And shutting down a facility or requiring the filing of an NDA may not always be in the public interest.

So which facilities should be subject to FDA oversight? There is no single ideal solution, but a potential framework could include some of the following: Volume of production. Clearly larger scale operations expose more patients to risks. Those risks are not mitigated by an after the fact prescription. Large-scale operations should be subject to GMP. The nature of the products, manipulating a sterile product is a high-risk activity. Sterile drugs made from nonsterile raw ingredients are especially high risk.

Expiration dates. The longer a product sits before use, the more likely it is to degrade or sustain bacterial or fungal growth. Longer beyond use dating calls for higher quality standards and may also serve as a mechanism to distinguish between traditional pharmacy and this new compounding sector.

My written testimony contains additional recommendations for a practical and enforceable framework. In particular, facilities under FDA oversight must be required to register and to avoid an unfunded mandate to pay a fee. Compounded drugs should be clearly labeled as such and wholesale distribution prohibited. Current law gives FDA the authority to create a list of drugs that may not be compounded and to inspect pharmacies as necessary, and these authorities must be maintained.

I thank you for your leadership on this important issue. It is time to update the FDCA to remove ambiguities and create a clear, workable framework for patient safety. And I welcome your questions.

Mr. PITTS. The chair thanks the gentleman.

[The prepared statement of Mr. Coukell follows:]

**Testimony before the Committee on Energy and Commerce
Subcommittee on Health
United States House of Representatives
July 16, 2013**

The Pew Charitable Trusts

Dear Chairman Pitts, Ranking Member Pallone, and members of the Subcommittee,

Thank you for the opportunity to testify on the need for federal legislation to improve the safety of compounded medicines.

My name is Allan Coukell. I am a pharmacist by training and director of drug and medical device work at the Pew Charitable Trusts, an independent, nonpartisan research and public policy organization. Pew has a longstanding focus on drug quality issues.

This subcommittee and the Oversight Subcommittee have held a number of hearings on compounding, and have heard extensive testimony regarding the risks to patients.

I won't reiterate those risks today, except to say that the recent fungal meningitis outbreak that has killed so many Americans is far from an isolated incident. There have been plenty of other deaths and injuries caused by compounded drugs, and there is ample reason for ongoing concern about quality problems at compounding pharmacies.

Today I would like to propose ways that Congress can reduce these risks and at the same time ensure that patients have access to the medicines that they need.

Current law is inadequate for this purpose, both because legal decisions have created uncertainty about the status of section 503A of the Food Drug and Cosmetic Act, and because 503A does not recognize the emergence of large-scale compounding operations that are important for patient care yet far removed from traditional pharmacy practice.

Let me begin with two points that all stakeholders should endorse.

First, patients, doctors and pharmacists should prefer FDA-approved drugs over compounded medicines whenever possible.

Only FDA-approved drugs go through pre-market review to establish safety, efficacy and bioequivalence, as well as pre-approval of manufacturing methods and facilities.

Any new legislation must not encourage compounding at the expense of traditional manufacturing.

Second, the preparation of customized medicines in response to a prescription for an individual patient is an established part of pharmacy practice. This traditional compounding is a matter for state jurisdiction, and must remain so.

Now allow me to make a third point, which is that there is a large-scale compounding sector that fits neither of the above categories. Instead it undertakes batch production of products—often high-risk sterile products—and admixtures of FDA-approved drugs for use in hospitals and clinics.

Indeed, according to a recent report by the HHS Inspector General, 85% of hospitals that administer intravenous drugs purchase some of these products from outside pharmacies.¹ This is true for hospitals of all sizes, in some cases accounting for thousands of doses per day.

Pew recently joined with the American Hospital Association (AHA) and the American Society of Health-System Pharmacists (ASHP) to co-host a Pharmacy Sterile Compounding Summit.²

This meeting included representatives of hospitals of varying sizes, purchasing organizations, compounders, regulators, and pharmacy associations.

It also included experts in pharmacy practice and drug manufacturing quality standards. These experts emphasized the enormous difference between the standards developed for traditional pharmacy practice and the Good Manufacturing Practices that apply to drug manufacturing. They emphasized that only GMPs are adequate to ensure the safety of large-scale standardized production, and that USP compounding standards, which some have suggested could be used as a national standard, were developed for use in pharmacies and are therefore not suitable for larger-scale production.

cGMPs, on the other hand, are developed to ensure the proper production of large volumes of repeated batches of medicines which require standardized processes. These are the appropriate types of quality standards for large-scale compounding.

For example, cGMP requires manufacturers to validate systems and processes to ensure that medicines meet consistent quality and safety standards. Process validation becomes increasingly important as the same drug is compounded in repeat batches. In addition, USP 797 does not require the testing of a drug's starting ingredients, while cGMP does. And expiration dates are set for a manufactured drug based on extensive stability testing. But a beyond-use date for a

compounded medicine may in some cases be set by referencing published studies of drugs that may not conform exactly to the compounded product.^{3,4}

Oversight of such standards is a role for the FDA, not for state boards of pharmacy.

Section 503A of the FDCA already recognizes the FDA's responsibility to oversee some compounding activities. 503A contains important elements to ensure that compounding not exceed traditional pharmacy practice, such as prohibiting the copying of marketed drugs. Importantly, it also gives the FDA the authority to create a list of drugs that may not be compounded.

However, merely reinstating section 503A would leave a lack of clarity about which facilities were subject to FDA oversight; moreover, it would not clearly give the FDA the ability to ensure that large-scale compounders comply with applicable GMPs.

Shutting down a facility or requiring an NDA may not always be in the public interest. As noted previously, a majority of hospitals now outsource some sterile production, repackaging, and admixture.

Drawing the line

Which facilities should be subject to GMP and therefore FDA oversight? It is a challenging line to draw, and there is no single ideal solution. A potential framework could build on the following factors:

- Volume of production. Clearly, larger-scale operations expose more patients to risks and are more amenable to the kinds of process measures that underpin GMP.
- Nature of the products. For example, sterile products, as a general matter, are higher risk than non-sterile (although the latter are not without risk) and sterile drugs manufactured from non-sterile precursors or bulk active ingredient are higher risk again than sterile repackaging or admixture that begins with FDA-approved sterile products.
- Percentage of sales. While an arbitrary sales threshold does not speak directly to risk, it is a potential mechanism that could help distinguish between traditional dispensaries that produce the occasional product and those whose business is based substantially on compounding.
- Expiry dates. Products used immediately or very soon after production are less likely to have undergone chemical decomposition or have sustained massive bacterial and fungal growth than products that sit on a shelf for a prolonged period before administration. Extended beyond-use dating calls for higher production and testing standards and may also serve as a mechanism to distinguish between traditional pharmacy and something different.

- Interstate sales. The sale of products across state lines has been proposed as a mechanism to distinguish between state- and FDA-regulated operations. This would ensure that some large entities would be under FDA jurisdiction. It would provide a measure of regulatory clarity in that states would be entirely responsible for drugs produced within their own boundaries. However, it would leave some very large operations under state oversight and, conversely, would sweep into federal jurisdiction some very small facilities that make some interstate sales.

Finally, let me address the issue of the prescription. One thing that characterizes pharmacy practice is that pharmacies fill prescriptions. Any business whose principal activity is the production of products without a prescription is not a traditional pharmacy.

Some have suggested that compounding pharmacies should be allowed to retroactively reconcile the product they sell with a prescription received later. While such a requirement might serve to limit the scale at which a compounder operates, it is would not be sufficient to distinguish between traditional pharmacy and this new, large-scale sector.

Additional considerations

There are a number of additional elements to an effective proposal that we urge Congress to include. First, the FDA and compounders alike must clearly know which facilities are subject to FDA oversight. Such facilities should be required to register with the agency and, to avoid an unfunded mandate, pay a fee. Facility inspections should be periodic with their frequency based on a risk-based schedule and, following a transition phase, this should include an initial inspection before new facilities come online.

Under this framework, states may continue to require FDA-registered compounding facilities to hold state pharmacy licenses, but state enforcement of quality standards should be preempted for these facilities.

Legislation should be clear that a compounder may not make a copy or a variation of a marketed drug, except when that drug is in shortage or to address specific medical needs of a specific patient. Congress should also prohibit the wholesale of compounded drugs. All compounded medicines should be clearly labeled as such.

Another important safeguard against circumvention of the approvals process is limiting compounding from bulk to only well-characterized and already in-use active ingredients, such as those described by a USP monograph, or those in an existing drug application. These concepts are not new, but are part of current 503A language.

Key safety requirements should also be set at the federal level, such as a “do not compound” list. Congress has already recognized that certain products are not suitable for compounding (frequently cited examples include transdermal delivery systems, biologic products and sustained release formulations) and has given the FDA authority to establish a “do not compound” list. This authority should be maintained and should apply to both FDA-registered and non-registered facilities, as it does now.

In order to enforce these important provisions, the FDA needs to be able to inspect compounding pharmacies to know if they are complying with the law, and not just after patients have received contaminated drugs. Currently, the FDA has the authority to inspect all pharmacy compounders, and that authority should not be weakened. The FDA should not be limited in its ability to access a site to cases where a state has voluntarily notified the agency of a pharmacy violation. Furthermore, the FDA should be given the authority to inspect pharmacy records for purposes of enforcing the “do not compound” list.

Conclusion

We thank you for your leadership on this important issue. Congress has long recognized the role of the FDA in providing oversight of compounding. It is time to update the Food, Drug, and Cosmetic Act to remove ambiguities and create a clear, workable framework to address patient safety.

Thank you for the opportunity to testify, and I welcome your questions.

References

¹ Office of the Inspector General, Department of Health and Human Services. “Memorandum Report: High-Risk Compounded Sterile Preparations and Outsourcing by Hospitals That Use Them, OEI-01-13-00150”. April 10, 2013. <https://oig.hhs.gov/oei/reports/oei-01-13-00150.pdf>

² Pharmacy Sterile Compounding Summit: summary of a stakeholder meeting. http://www.pewhealth.org/uploadedFiles/PHG/Content_Level_Pages/Other_Resource/Compounding_report.pdf

³ United States Pharmacopoeial Convention. USP–NF General Chapter <797> Pharmaceutical Compounding—Sterile Preparations

⁴ 21 CFR 211. Current good manufacturing practice for finished pharmaceuticals

Mr. PITTS. Dr. Miller, you are recognized for 5 minutes for your opening statement.

STATEMENT OF DAVID G. MILLER

Mr. MILLER. Good afternoon, Chairman Pitts, ladies and gentlemen of the committee, it is a pleasure on behalf of the International Academy of Compounding Pharmacists to appear before you today to talk about a situation that started with one pharmacy in Framingham, Massachusetts, but fundamentally has uncovered a real gap in our laws.

Now, I have been listening this afternoon to testimony, and you have the written testimony of my colleagues and myself, but I have heard six different terms used to define this thing that we are attempting to address and regulate.

Members of the International Academy of Compounding Pharmacists are pharmacists. We work in small drug stores, we work in large chain drug stores, at CVS, at a Publix grocery store in Florida, in hospitals.

Compounding is an essential core component of the filling and care of prescription medications for patients throughout this country. One of the challenges that we have found ourselves in is that the core concept of filling a prescription ordered by a physician either for the treatment of that patient in his or her home, or the use of that medication in the doctor's office for administration and treatment of a patient on site has somehow been clouded by the evolution of this other thing.

Tonight, this afternoon, we have heard that thing referred to as repackagers, traditional compounders, nontraditional compounders, outsourcing pharmacies, outsourcing admixture pharmacies, manufacturers, compounding manufacturers, batch production.

Now, again, I am a pharmacist. I look at this relatively simple. I get a prescription from a physician to take care of an individual patient, or I get a prescription to send a medication to a doctor's office so he or she can take care of that patient. IACP believes that currently section 503A is very clear that the Food and Drug Administration does have authority over the distribution of drugs in the United States, either through manufacturing or wholesaler distribution, and that our States have authority over the practice of pharmacy.

We believe at IACP that a great deal of confusion over this other entity that appears to not want to be regulated either by the FDA or falls within the gap of the regulation of the States, that is a separate group from pharmacy. And one of the things that we have seen as we have looked and worked with the Senate HELP committee on S. 959 is the core concept of preserving the integrity of the drug distribution system under FDA oversight, and on that side of the body it has been deemed a compounding manufacturer, unfortunately has gotten into the day-to-day practice of pharmacy and practice of medicine.

For example, on the Senate side, we now know that one of the things that we must have to ensure the protection, the safety and access of medications for patients is quality assurance. There is no language in S. 959 requiring all pharmacies or these other things

to adhere by the nationally published standards of the United States pharmacopeia. There is no quality assurance.

There are specific language that intrudes on the practice of medicine and the practice of pharmacy. Most recently, the version of S. 959 that was distributed now includes a requirement that a pharmacist who fills a medication that may be a medication that is in drug shortage must inform the Food and Drug Administration within 3 days of filling that prescription. And we believe that is a significantly troublesome precedent.

There are also questions about whether or not all pharmacies would be actually required to participate and be overseen under this process and indeed within Senate 959 as my colleague from NCPA said previously, all hospitals and health system pharmacists are actually exempted from the Senate's new approach to regulating this issue.

Fortunately, Congressman Griffith has introduced a draft piece of legislation that we believe is really the closest solution to solving the questions that arose because of NECC's activities. We look forward to continuing to work with him and with this body on helping craft legislation that does a few most critical things: One, preserve patient access to medication; two, assure the American public of the safety of the medicines that they receive, that there are swift and accountable actions by our regulators at both the State and the Federal level to carry those laws out.

Thank you very much.

Mr. PITTS. The chair thanks the gentleman.

[The prepared statement of Mr. Miller follows:]



**Testimony of David G. Miller, RPh., CEO and EVP of the
International Academy of Compounding Pharmacists (IACP)
“Reforming the Drug Compounding Regulatory Framework”**

Tuesday, July 16, 2013, 3:00 p.m.
2123 Rayburn House Office Building

Good afternoon Chairman Pitts, Ranking Minority Member Pallone and Members of the Health Subcommittee, I am pleased to have this opportunity to be before you today to discuss a number of legislative proposals that attempt to address the tragedies that have occurred as a result of the New England Compounding Center (NECC) and their role in distributing contaminated steroid medications that ultimately resulted in patient deaths and illnesses across the country. I share your concerns that we do everything possible to prevent a future such scenario and have dedicated the majority of my time for the last 10 months to working in a bi-partisan fashion to achieve a balanced and targeted solution to close existing loopholes in federal statute that may assist in this goal.

IACP is an international, professional association established in 1991 to protect, promote and advance the art and science of pharmacy compounding. IACP provides support to more than 2,100 members through programs and services including reimbursement/third-party advocacy, government

representation, regulatory analysis, public relations support, referral services and a fellowship program. IACP also represents more than 185,000 patient and practitioner advocates as part of our grassroots contact network.

I know that, today, you have asked me to comment on three legislative proposals, in particular: S. 959, “The Pharmaceutical Compounding Quality and Accountability Act, introduced by Senate HELP Committee Chairman Harkin (D-IA) and Ranking Minority Member Alexander (R-TN);” H.R. 2186, “Verifying Authority and Legality In Drug (VALID) Compounding Act of 2013,” introduced by Congressman Ed Markey (D-MA); and a draft bill currently being drafted by Congressman Morgan Griffith (R-VA) and several members on the Democratic side of the committee.

IACP has been working diligently with Senate HELP Committee staff for months to reach a pragmatic and appropriate legislative response focused on mitigating situations such as those which led to the NECC tragedies. Despite this lengthy negotiation and discussion process, IACP continues to have some major issues with the recently reported version of S. 959, “The Pharmaceutical Compounding Quality and Accountability Act,” which we understand the Senate may consider prior to the August congressional recess.

While IACP continues to work with Senate staff to further refine the bill, I must express our substantial concerns about the direction and substance of the latest version of the legislation shared with IACP. We readily acknowledge and are appreciative of the fact that the staff and members of the U.S. Senate’s Committee on Health, Education, Labor and Pensions have worked diligently and

cooperatively for several months with the various stakeholders in the pharmacy and practitioner communities to draft legislation to address the tragic patient deaths and illnesses associated with the New England Compounder Center (NECC) and its illegal activities.

In reviewing the Committee's most recent version of S. 959, I wanted to make you aware of several provisions with which (in addition to those provisions about which we have previously stated strong concern and/or opposition to with committee staff both verbally and in writing) IACP has concerns.

A primary concern IACP has with the bill is a provision that will dramatically impact the practice of pharmacy compounding and severely limit anticipatory compounding only in instances where the historical volume is directly associated with an individual patient prescription. This provision would seriously curtail the ability of a pharmacy to have product on hand when demand exists and would limit the opportunity of the pharmacist to perform sterility and other testing of these medications while also meeting the emergent needs of the patient.

Language in the latest draft of the bill also does not clearly preserve the ability of prescribers, such as physicians, to order office-use medications. That omission would appear to eliminate a necessary category of production of compounded medications. While most compounded products are produced in response to a prescription for a specifically named patient or individual, office-use compounding remains vital to the health and safety of the public.

Additionally, even long-standing industry safety standards (chapters 795 and 797 of the U.S. Pharmacopoeia (USP), which are largely followed by compounding pharmacies) have been removed from an earlier draft of the bill. USP standards are protections that are broadly supported by and observed in the compounding pharmacy industry, which is regulated by state boards of pharmacy.

Another area of major concern for IACP is the fact that certain sectors of the health care industry have been exempted from the very same standards that must be achieved by compounding pharmacies and “compounding manufacturers.” IACP is concerned that patients who receive compounded medications made in a hospital setting or from a mail order pharmacy – a frequent occurrence – are not guaranteed the same safety standards as those who receive compounded medications from a pharmacy.

This should not be the goal of a bill allegedly about patient safety – to allow a carve-out for certain special interests – because it is simply not in the best interest of patient care. With these carve-outs, there will continue to be a patchwork of safety requirements that will not be consistent or equally protective for all patient populations.

The goal of any bill addressing the NECC issues should be to balance the need to strengthen the federal law while preserving the ability of health care practitioners to prescribe much-needed compounded medications. Most importantly, the bill should focus on the protection and safety of all patients and the public.

Of greatest concern to IACP is the fact that one of the fundamental documented problems in the NECC scenario was inaction by the Massachusetts Board of Pharmacy and the federal Food and Drug Administration (FDA) in addressing a situation where they had made numerous visits to the facility and had knowledge of significant problems. Despite that, they did not shut NECC down and this bill does not provide for any reporting system for the FDA, or hold the agency accountable in any other way. This is a significant flaw with this bill that has yet to be addressed.

IACP continues to believe that S. 959 has become weighted down with competitive issues that have been added to appease certain sectors of the commercial pharmaceutical industry, which have nothing to do with safety issues. Our members continue to have serious concerns with several provisions in the current legislation that we believe will unnecessarily obstruct the practice of pharmacy compounding and patient access to vital compounded medications.

IACP remains hopeful that that the Senate will address these concerns before the bill goes to the Senate floor for a final vote. Without significant changes the IACP will have no choice but to oppose S. 959. We hope to continue to work with the Committee to produce a fair and balanced piece of legislation that protects patient safety while at the same time fully preserving the ability of pharmacists to compound life-saving medications for patients.

With regard to the proposed House legislation entitled "Verifying Authority and Legality in Drug (VALID) Compounding Act of 2013," (H.R. 2186), introduced by Congressman Ed Markey (D-MA), IACP has not taken an official position, but is happy to generally comment on the legislation.

As proposed, IACP reads H.R. 2186 to maintain state authority for traditional compounding activities, while giving sole authority to the FDA in the task of regulating interstate commerce and pharmacies engaging in “high-risk” sterile compounding. The bill also would provide the FDA with sole regulatory authority over compounding pharmacies that engage in interstate commerce and high-risk sterile compounding without receipt of or in advance of a prescription.

The VALID Compounding proposal would mostly preserve state regulatory authority for traditional small compounding pharmacies. This is an area that should not be further defined or micromanaged from the federal level, as all pharmacies have (in the past) been regulated by their State Boards of Pharmacy and IACP believes that is where the regulatory authority for traditional pharmacies should remain in its entirety.

The VALID Compounding Act provides for an exemption from certain FDA requirements (similar to the existing 503 (a) section of the FDCA) if compounding pharmacies meet specific conditions, such as:

- The drug must be compounded by a licensed pharmacist or physician for an identified patient with a prescription for the drug;
- The drug must be compounded using safe and approved ingredients and practices (this would be a new and somewhat arbitrary condition – what are “approved practices” and

who defined them and which standards (either existing or yet to be proposed) would satisfy this requirement; and

- The drug cannot be a copy of a commercially-available drug, except in cases of a drug shortage.

As IACP reads H.R. 2186, we believe that the bill allows compounding pharmacies to compound drugs before receiving prescriptions for the drug provided that they register with the FDA and meet specified safety standards (IACP questions what these standards will be – will they be the same standards that large pharmaceutical manufacturing companies must meet or – more appropriately – focused on the nature of the compounding business and its practitioner and patient needs) and allows “capable” State regulators to oversee these pharmacies. Again, IACP questions who would be qualified to determine who is or is not a “capable” state regulator – this is extremely arbitrary and confusing language in the bill.

The VALID Compounding Act also requires the FDA to define requirements (i.e. safety, testing, inspection, reporting or other requirements) for types of compounding pharmacies that wish to compound drugs before or without receiving a valid prescription for an identified patient. This provision of the bill would make all anticipatory compounding and “office use” compounding (even with a doctor’s order) essentially an act of manufacturing. This requirement conflicts dramatically with current pharmacy practice and practitioner and patient needs.

The VALID Act proposed legislation also requires the FDA to share any information gathered during inspection of a compounding pharmacy with the State where the pharmacy is located and any States into which the pharmacy ships, and requires FDA to share its lists of drugs that cannot be compounded and bulk ingredients that can be used to compound drugs, with State regulators. For the most part, IACP supports this provision in the bill, as it establishes some accountability for the FDA in communicating with states about potential problems with pharmacies. The Senate bill, S. 959, does not achieve similar oversight and accountability.

The Markey bill also would increase transparency to patients and consumers. Under the bill, compounded drugs must be labeled to ensure that recipients are aware that they are receiving a compounded drug and to provide a means to report serious adverse drug reactions. IACP has long been supportive of such labeling requirements and has encouraged its members to openly do so when dispensing a compounded medication.

Pharmacies that are made aware of serious adverse events are also required to report that information to the FDA. The VALID act also creates a petition process allowing the public to submit to the FDA drugs that should or should not be compounded because of a public health need or risk. IACP makes the current FDA “do not compound” list readily available to its members. The only problem is that the FDA list has not been updated in over 10 years. IACP would support an open opportunity for public and the medical community input on such issues, but would also like to see the FDA have a regular mandated window for updating this list.

Overall, IACP believes that there is merit to certain provisions of the proposed “VALID” Act, but believes that the way the bill treats office use and anticipatory compounding is problematic and will cause major patient and practitioner access issue for medications that are not manufactured and readily available. This is a core concern for IACP, its members and its patient and practitioner advocates.

Finally, I am pleased to say that IACP believes the bill that comes closest to ensuring accountability for agencies with oversight authority and for maintaining patient and practitioner access is the draft Griffith bill that was circulated (not in its entirety) last week. IACP has had the opportunity to provide input into the bill on both the Republican and Democratic sides of the aisle and believes the draft legislation we have seen seems to address some of the most obvious problems that led to and exacerbated the NECC outbreak.

Under the draft Griffith proposal, the bill makes it clear that a compounded drug is not subject to the provisions of the Federal Food, Drug and Cosmetic Act (FDCA) addressing adulteration and the need to adhere to “current good manufacturing practices (cGMPs); misbranding and the need to provide “adequate directions for use” and new drugs, as long as the following conditions are met:

- The drug product is prepared by a licensed pharmacist or physician in response to a valid prescription for an identified individual patient; or
- If prepared before the receipt of such prescription, the drug product is made only in “limited quantities” and in response to a history of the licensed pharmacist’s or physician’s

receipt of valid prescription orders for that drug product within an established relationship between the pharmacist, the patient, and the prescriber; or

- If prepared pursuant to a non-patient-specific purchase order, the drug product must be administered by a health care practitioner within a physician's office, hospital, or other health care setting. Additionally, patient-specific valid prescription information for the drug product must subsequently be provided to the pharmacist within a week and account for all of the compounded medications received. This allows for practitioners who do not have a patient name in advance, will be able to properly treat a patient and then send in patient information subsequent to their treatment.

Although not yet completely clear, IACP supports the fact that the draft bill does not attempt to step on the authority of states – many of whom have office use and anticipatory compounding regulations in place – by deferring to the state if such language exists. IACP feels that this is very important as activity has occurred in almost every state subsequent to the NECC outbreak – many positive actions that are aimed at safety and access issues.

IACP is also supportive of language that would require that the drug product be compounded using bulk active pharmaceutical ingredient that:

- Complies with either an applicable United States Pharmacopoeia (USP) or National Formulary (NF) monograph, is part of an FDA-approved drug, or appears on a list established by the HHS Secretary;
- Manufactured in an FDA-registered establishment; and
- Accompanied by a valid certificate of analysis.

Additionally, the draft bill would require the Secretary to develop and implement a system, in consultation with the National Association of Boards of Pharmacy, for receiving and reviewing submissions from State boards of pharmacy on actions taken against compounding pharmacies. This is a critical factor in gathering knowledge of and enabling the proper authorities to address potential problems before they worsen.

Also, the bill requires that - prior to issuing regulations addressing the listing of drug products that may be compounded with no existing monograph, or that may be unsafe, ineffective, or too difficult to compound, the Secretary must convene and consult with an advisory committee, unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health. The advisory committee must have representatives from the NABP, USP, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary.

The Secretary must update the lists identified above regularly, but not less than once each year. This is something that IACP has long sought.

Overall, it seems like the Griffith draft bill is going in the right direction in terms of ensuring accountability, access and the safety of compounded medications. IACP believes this approach addresses the problems that led to the ultimate result of the NECC tragedies. It balances all factors that could, potentially, mitigate a future similar scenario. The bill draft keeps the language focused on the issues at hand and has not become a “Christmas tree” bill that includes anti-competitive and non-germane language having nothing to do with the safety of compounded medications.

I would be happy to answer any questions you may have at this time and respectfully ask that my testimony be submitted for the record. Thank you for giving me this opportunity and we look forward to continuing our work with the Subcommittee and full Committee on reaching a positive and workable resolution to this crisis.

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Mr. PITTS. Dr. Catizone, you are recognized for 5 minutes for your opening statement.

STATEMENT OF CARMEN CATIZONE

Mr. CATIZONE. Good afternoon, Chairman Pitts and members of the subcommittee. On behalf of the National Association of Boards of Pharmacy and the State boards across the country, thank you for the opportunity to be here today.

NABP believes that the three legislative proposals provide the regulatory framework for us to address the issue of compounding manufacturing and to protect the public health. We support the Senate HELP bill and support the provisions that clearly distinguish traditional compounding, which should be regulated by the States and remain the purview of the States, and manufacturing, which should be the purview and remain the purview of the FDA. And we support the new category of compounding manufacturer that should fall within the purview and under the regulation of the FDA.

We commend Mr. Griffith and the other authors of the House bills for their diligence and concern for patient safety. However, we must also caution that there are provisions in the House bills that may not be intended to but could take us in the wrong direction, in a direction different from the legislative intent and a direction that could lead us to another NECC tragedy.

In regard to a primary issue identified by the House bill, NABP agrees that there is a bona fide but narrow need for pharmacists to compound a limited amount of products for administration to patients. The creation of the previously referenced third category, compounding manufacturer, seems to address the needs of the majority of patients. However, we are also sensitive to the fact that some stakeholders do not believe this is an appropriate category for this activity and would like to place this activity under the domain of traditional compounding and the purview of the State boards of pharmacy.

To respond to these concerns, specifically those of patient need, limiting the amounts of compounded products for direct administration in order to avoid any masking of manufacturing for compounding, we would support such an allowance provided there are limitations and qualifiers to those activities.

Those qualifiers include: First, the State has to allow such activity. Once that is allowed, the other limitations follow. There must be a demonstrated medical need for the compounded product. A non-patient-specific order must be written by the practitioner who will be administering or is directly responsible for administering the compounded product.

The total quantity provided at the clinic office or healthcare setting per patient cannot exceed a 10-day supply. The compounded medication cannot be resold. The compounded medication must be prepared in accordance with applicable USP standards or GMPs, depending upon the product, as determined by the FDA.

There must be a limitation on the total quantity of compounded products that the pharmacy can prepare. Such quantity cannot exceed a certain percentage of or some other measure of the phar-

macy's total number of prescriptions dispensed, dosage units, patient supply, or some other measurable and comparable factor.

The pharmacy must notify the applicable State board or boards of pharmacy and FDA of their involvement in this area in accordance with an appropriate process and frame times to be determined. And the FDA must have full legal access to all records of the pharmacy engaged in this activity. And equally as important, there can be no prohibitions on the sharing of information between the States and the FDA on these activities, as presently exists.

We want to note that these limitations and qualifiers for this activity does not erode the distinction between compounding manufacturing and compounding manufacturers created by the Senate HELP bill. They simply allow for an exemption with additional oversight under the category of traditional compounder.

Generalizing to a large extent, if the Senate HELP bill is used as a framework and modification from the House bills are employed, we would have three broad categories for compounding and manufacturing.

Traditional compounding: Per patient, patient-specific, regulated by the States, and all requirements of the States and USP standards in place. The FDA's current enforcement authority and responsibilities would remain. And the FDA could act, as they have been able to act, in the recent past.

Manufacturing and compound manufacturing: regulated by the FDA, complete access to all of those records, all of the requirements of the FDA, including GMPs.

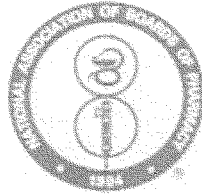
And then this exemption, under traditional compounding: for those activities for administration within a clinic, healthcare setting, or hospital, shared authority between the FDA and the States, access to those records, and communication between the FDA and the States.

In closing, we appreciate the opportunity to be here today. We respectfully request that action be taken to develop and pass Federal legislation. We think it is important. We don't want to lose the opportunity.

Thank you.

Mr. PITTS. The chair thanks the gentleman.

[The prepared statement of Mr. Catizone follows:]



Testimony
on behalf of the
National Association of Boards of Pharmacy

Before

House Energy and Commerce Committee
Subcommittee on Health
United States House
July 16, 2013
Hearing on
Reforming the Drug Compounding Regulatory
Framework

Presented by:

Carmen Catizone, M.S., RPh, DPh
Executive Director
National Association of Boards of Pharmacy

Good afternoon Chairman Pitts, Ranking Member Pallone, and members of the Subcommittee. I am Carmen Catizone, executive director of the National Association of Boards of Pharmacy (NABP). NABP appreciates the opportunity to appear before you again, today and provide information related to the various proposed bills concerning the regulatory framework for pharmacy compounding.

NABP is the impartial organization founded in 1904 whose members are the state agencies that regulate the practice of pharmacy. NABP supports the state boards of pharmacy by developing, implementing, and enforcing uniform standards for the purpose of protecting the public health. NABP also helps state boards of pharmacy to ensure the public's health and safety through its pharmacist license transfer, pharmacist competence assessment, and accreditation programs.

NABP believes that the three pending legislative proposals can provide the regulatory framework needed to protect the public health as well as identify and answer the complex questions surrounding pharmacy compounding and manufacturing. NABP supports the "Pharmaceutical Compounding Quality and Accountability Act" proposed by Senator Harkin and the United States Senate Committee on Health, Education, Labor, and Pensions (HELP). The proposed legislation addresses the critical concerns identified by the states and validated by NABP through its inspections of compounding pharmacies. As provided in the proposed Senate legislation, NABP agrees that the regulation of the practice of pharmacy, which includes traditional pharmacy compounding, remains the responsibility of the state boards of pharmacy and manufacturing remains the responsibility of the Food and Drug Administration (FDA). NABP supports the establishment of the new category of "compounding manufacturing" regulated by FDA, and supports the clear distinction between this new category and traditional pharmacy compounding. The Senate Bill addresses and outlines all of the major areas that need to be considered in federal legislation. NABP discussed with the Senate HELP Committee concern with the proposed exemption for intrastate distribution of non-patient-specific sterile compounded products. We understand the logic of establishing a delineation point to more readily identify and regulate large-scale operations that conceivably pose more risk to patients than smaller operations. However, as we explained to the Senate HELP Committee, it is our finding that non-patient-specific, sterile prepared products distributed within a state bear the same risk levels to patients as products that are introduced into interstate commerce. The differentiation between intrastate and interstate activities to define a compounding manufacturer could create patient safety concerns by allowing large-scale intrastate entities to avoid federal regulation. We indicated to the Senate HELP Committee that although this is a critical concern for the states, NABP would support the proposed legislation absent this revision, if our concern is noted and the situation monitored for any additional future action that may be necessary.

The House proposals identify significant areas of concern where consensus may be lacking and further clarification is required. To that extent, NABP favors modification of the key provisions of the "Verifying Authority and Legality in Drug Compounding Act of 2013" and the "Compounding Clarity Act of 2013" to coincide with the desired outcomes shared by all of the interested stakeholders and to build consensus on the remaining, unresolved issues.

We commend the authors of the House bills for their diligence and concern for patient safety and believe that their efforts provide mechanisms for moving forward on some of the more difficult

challenges of this entire issue. We must also caution that some provisions within the House bills may have the undesired effect of moving the regulatory framework in a different direction than is needed to correct the deficiencies and problems identified by the NECC tragedy. Additionally, those provisions could unwittingly create an opportunity for manufacturing to occur under the guise of compounding and even more disconcerting, cause the recognition of such activity as permissible under federal law. To some degree, passage of those provisions will surpass existing exceptions that led to the present situation and recognized need for federal legislation.

NABP agrees that there is a bona fide, but narrow, need for pharmacists to compound a limited amount of products for administration to patients. The creation of the previously referenced third category, compounding manufacturer, seems to address the needs of the majority of patients. However, NABP also understands that some stakeholders do not believe that this is an appropriate category for such activity and are seeking an approach to allow for such activity under traditional compounding and the purview of the state boards of pharmacy.

To ameliorate these concerns – specifically those of patients needing limited amounts of compounded products for direct administration in clinics, offices, and other health care settings and under restricted circumstances, NABP would support the allowance of such activity under the domain of traditional compounding provided limitations and qualifiers are in place to assure that the activities are safe and simply not a masquerade for manufacturing.

Limitations and qualifiers for traditional compounders that have been discussed with NABP and that we submit for the Subcommittee's consideration include:

1. There must be a demonstrated medical need for the compounded product.
2. The non-patient specific order must be written by the practitioner that will be administering, or is directly responsible for administering, the compounded product to the patient.
3. The total quantity provided to the clinic, office, or other health care setting cannot exceed a 10-day patient supply.
4. The compounded medication cannot be resold by the clinic, office, or other health care setting.
5. The compounded medication must be prepared in accordance with applicable USP Standards or Good Manufacturing Practices (GMP's) depending on the product, as determined by the FDA.
6. There must be a limitation on the quantity of compounded products that can be produced. Such quantity cannot exceed a certain percentage of, or some other measure of, the pharmacy's total number of prescriptions dispensed, dosage units, patient supply, or some other measurable and comparable factor.
7. The pharmacy must notify the applicable state board(s) of pharmacy and FDA of their involvement in this area in accordance with an appropriate process and time frames to be determined.
8. The FDA must have full legal access to all records of the pharmacy engaged in this activity and there can be no prohibitions on the sharing of information between the states and FDA on these activities.

NABP wants to note that these limitations and qualifiers do not erode the distinction between compounding and manufacturing provided by the three categories of activity noted in the Senate bill. They simply allow for an exception, with additional oversight, under the category of traditional compounder. NABP believes this modification is critical to maintain the present authority of the states and address one of the contributing factors to the NECC crisis, the ambiguous authority between the states and FDA. Legislation specifying that a compounding manufacturer cannot be licensed as a pharmacy must remain because it is essential to distinguishing between state-regulated compounding and FDA-regulated manufacturing. The allowance for non-patient compounded products for administration would recognize this distinction and also address one of the concerns voiced by the FDA – the need to access state-licensed pharmacy records to help determine whether such pharmacy is engaged in activities that should be overseen by FDA.

The recognition and separation of activities and authorities would apply as follows:

1. A traditional compounding pharmacy would only be engaged in patient specific compounding thus meeting the definition of compounding within the practice of pharmacy as defined by states. It would operate under the authority of the state board of pharmacy, could not license or register as a compounding manufacturer or as a manufacturer, and would be subject to all laws, regulations, requirements, records access, and inspections required by the state board of pharmacy. If the FDA had sufficient information to suspect that the pharmacy was violating federal law or engaged in manufacturing either as a manufacturer or compounding manufacturer, it could employ the enforcement means currently available to access records and gain entry into the pharmacy. Cooperation between the FDA and applicable state board(s) of pharmacy would also need to occur.
2. If the entity was operating and registered with the FDA as a manufacturer or compounding manufacturer, it would be responsible to the FDA and its laws, regulations, records access, and inspection requirements. If a state had sufficient information to indicate that the entity was violating state laws/regulations, it could employ the enforcement means currently available to the state as well as work cooperatively with the FDA.
3. If a traditional compounding pharmacy is engaged in non-patient specific compounding for administration with the limitations and qualifiers identified above, then it would be subject to the authority of both the state board of pharmacy and the FDA. As such, the pharmacy would need to license with the state as a pharmacy and comply with all of the corresponding laws, regulations, and requirements as well as complete a notification process or registration with the FDA. Such notification or registration would result in compliance with applicable federal laws and requirements and FDA access to the pharmacy's records in order to help determine if the pharmacy's activity was exceeding the boundaries of traditional compounding and instead manufacturing.

Conclusion

NABP respectfully requests that action be taken to develop and pass federal legislation to create the regulatory framework so desperately needed to address pharmacy compounding and manufacturing concerns. The opportunity to correct a serious problem and protect patients from harm is here and should not be lost. We stand ready to assist in any way we can to reach consensus provided that patient safety is not circumvented by consensus.

Thank you.

Mr. PITTS. Thanks to all the witnesses for your opening statements.

We will now begin questioning. I will recognize myself for 5 minutes for that purpose.

Mr. HOEY, the meningitis outbreak was a clear example of a communication breakdown between the FDA and the boards of pharmacy. How does Mr. Griffith's draft address strong lines of communication between boards of pharmacy and the FDA?

Mr. HOEY. Thank you, Chairman Pitts.

I think one of the key things that it does is that it requires the FDA to respond within 60 days when the board of pharmacy has sent a complaint or sent some kind of a warning to the FDA.

Clearly, that did not happen in the NECC tragedy. Despite numerous heads-up, numerous warning signs sent to the FDA, there was not appropriate action taken. Representative Griffith's bill would require that action be taken within that 60-day period.

Mr. PITTS. Mr. Francer, the Senate bill establishes a third category: compounding manufacturers. Do you think establishing a new category would provide clarity or confusion?

Mr. FRANCER. Chairman Pitts, we believe that a new provision like that would provide confusion and that it is not necessary. We believe that traditional compounding as it is now should be regulated by the States. And when there is not a prescription and we have a large-scale-type facility, it is manufacturing. And the FDA is quite good at regulating manufacturers.

Mr. PITTS. Mr. Gaugh, supporters of creating a compounding manufacturing category argue that the growing market from hospitals for outsourcers necessitates a need to exempt them from the new drug requirements of the FDCA.

Wouldn't this change permanently preclude the FDA from requiring pre-inspection of some facilities engaged in large-scale manufacturing from bulk API?

Mr. GAUGH. It very well could. So it is not totally clear, but, to your point, yes, it could blur those lines.

And even if you do outsource the product from a hospital to another provider, you still have that capability in 21st-century electronics to provide that prescription for the patient to the compounding pharmacy to compound that product one by one, patient to prescription.

Mr. PITTS. Now, in your testimony, you write about the importance of the drug manufacturing control processes written into the ANDA applications. Can you outline why this process between FDA and an applicant is critical to ensure the safety and efficacy of the product that will be ultimately marketed to the public?

Mr. GAUGH. Yes. As I said earlier in my statement, the fundamental principles of quality can't be inspected and tested with the finished product. They need to be designed into that product and into the manufacturing process. And so the NDA and ANDA holders, as they develop these products, are designing that in for both the product and for the manufacturing process. That is not being done in compounding.

Additionally, the ANDAs and NDAs that are filed contain specific specifications around stability, around impurities, around container

closure, other manufacturing processes that, again, are not addressed by the compounding pharmacies.

Mr. PITTS. Dr. Miller, a couple of questions for you. Can you explain the importance of traditional compounding in our Nation's healthcare system? And then would you explain your thoughts on the creation of an expanded do-not-compound authority list for the FDA?

Mr. MILLER. Yes. Thank you, Mr. Chairman.

I think the easiest way to understand why we need compounded medications is just to look at all of us in the room. We are all different sizes, we are all different ages, we are all different sexes, and each one of us metabolizes and uses drugs in different ways. One of the advantages of having trained pharmacists and physicians who understand the use of having medications customized to each one of us, it helps us get the therapy that we need.

The U.S. drug system is phenomenal. The vast majority of the products manufactured by my colleagues at PhRMA and the Generic Pharmaceutical Association meet most of our needs. But some of us require tweaks. So compounding pharmacists use techniques, tools, skills, and training to prepare medicines that are unique to a particular individual. Or, in some instances, as we have heard repeatedly this afternoon and I know that you will hear over and over again, compounding pharmacists in the short term can step in to fulfill drug-shortage or backorder situations. That is first and foremost why we need compounds.

Your question was, the second one?

Mr. PITTS. Your thoughts on the creation of an expanded do-not-compound authority list for the FDA.

Mr. MILLER. IACP's position on this has been fairly consistent, sir. The FDA has had the authority to create a do-not-compound list based on a concern of safety or efficacy, and that we would leave in and strongly support.

Unfortunately, the agency has not updated that list in more than 10 years, and the provision of expanded authority to say, well, we can add a drug based on that it is hard to compound, or, you know, we think that you shouldn't use this particular active pharmaceutical ingredient—there are some other clauses on the Senate side—IACP strongly disagrees with that.

Because the fundamental reason for having a do-not-compound list is the agency should simply say, this medication is not safe, should not be used, is ineffective, it goes on the list.

Mr. PITTS. My time has expired.

The chair recognizes Mr. Green for 5 minutes for questions.

Mr. GREEN. Thank you, Mr. Chairman.

Dr. Thompson, in your testimony, you note that none of the classifications of "repackage" or "pharmacy" or "manufacturer" fits neatly with the regulatory needs of the large-scale compound or outsourcer.

Do you believe that asking the FDA to regulate these operations as manufacturers but leaving these specifics on how they are regulated up to the enforcement discretion of the FDA is a good policy?

Mr. THOMPSON. Sir, you know, reflecting on the Senate bill and how they have defined a compounding manufacturer, they defined

it as an entity that is not preparing product in response to a prescription, is engaged in interstate commerce, as a proxy for risk.

We think as this industry has evolved over the last decade to provide necessary service to hospitals and clinics and others that it has really created this gray area that there isn't Federal legislation or regulation for. So we do think it is necessary to help clarify what those entities do, which provide very helpful services to healthcare organizations and patients.

Mr. GREEN. Have you looked at the enforcement discretion that is in Congressman Griffith's bill?

Mr. THOMPSON. Well, we don't think enforcement discretion is a good policy. And that is the thing now, that there are these companies out there that are selling products for anticipatory use that, under the law, really isn't allowed. But they do fill a need. They are doing it under, you know, under good standards in many cases, but those need to be clarified.

What we think in the Griffith draft, that, you know, in some ways, it creates a third category without calling it that. It still allows entities to prepare large-scale products without Federal oversight. It leaves it to State boards of pharmacy—really, the same environment that exists now, that caused NECC—it leaves it to the State boards to call the FDA and identify something. The State boards are under-resourced, they don't have the expertise, and they are not manufacturing-level inspectors.

Mr. GREEN. And I agree, although I think the Griffith bill also has some enforcement at FDA to respond to those State boards when they just send a letter. Because we had a number of letters in this situation that was done.

Mr. MILLER, do you believe that using interstate commerce of sterile compounds in advance of a prescription is an adequate proxy to assess the highest-risk products?

Mr. MILLER. We have to be very careful with that, because as Congressman Griffith has pointed out in his own State and even here within the Washington, D.C., metro area, where I grew up in northern Maryland, the concept of interstate commerce as the end-all-be-all definition of when something goes over that line, we have to recognize that health care in the United States is not limited to within State borders. So I would challenge our thinking that just the movement of a medication across a State line should be the trigger for FDA oversight.

Mr. GREEN. OK.

Mr. MILLER. The other portion—

Mr. GREEN. I only have 2 minutes left. But I understand that, because, you know, people in Beaumont, Texas, people come from southeast Louisiana to buy from a pharmacy. But me, as an individual, I can do it. But if you are selling across, there may be an issue.

But let me go on to another question. Of your members, how many are unquestionably small operations that would be caught up in a regulatory net created by establishing a proxy of interstate sterile and anticipatory compounding?

Mr. MILLER. Quite honestly, sir, we don't know. And we don't know because there is very little data on the amount of prescription compounding that occurs not only in compounding specialty

pharmacies but hospitals, home infusion, long-term care, others. That data is unknown. This could have significant impact on practice.

Mr. GREEN. The goal of this legislation would be primarily to protect the health and safety of our people and to also respect the various State laws in providing regulatory certainty to those who are regulated and to those who are purchasing regulated products.

And I agree—some of us, I know the chairman has experience in State legislature. And we dealt with ours in Texas just like they dealt with in Pennsylvania. To me, our boards of pharmacy are certainly best equipped to regulate State agencies and the State-level activities.

However, don't you agree that engaging in interstate commerce creates a regulatory gray area that justifies a Federal response?

Mr. MILLER. Well, you have to look at the model that has already been created by my colleague at the National Association of Boards of Pharmacy for the transfer of licenses between pharmacists across State lines. There is certainly a public-private partnership that can exist that currently shares information back and forth as pharmacies, say, in Texas wish to be licensed in the State of Louisiana.

We don't necessarily believe that a Federal response is the only workable solution.

Mr. GREEN. Well, and I think you are right, that it has to be a combination of State and Federal. But, you know, the problem we had in Massachusetts wasn't going across into Connecticut, necessarily. It was actually going across the country. And, again, traditional compounding is something we want to protect.

I know I am out of time, Mr. Chairman. Thank you.

Mr. PITTS. The chair thanks the gentleman and now recognizes the gentleman from Virginia, Mr. Griffith, for 5 minutes for questions.

Mr. GRIFFITH. Thank you very much, Mr. Chairman.

I would say up front that I don't believe that our bill would have allowed the NECC situation to have occurred. I think the increased communications and the aspects that this bill has in it would have prevented that.

I do think that there are some things that we left holes in there and we are trying to sort out, and I think that is important. I also want to make it clear that if there is any indication, we can always tweak the language. That is why it is a draft bill. We are not trying to take anything away from the current FDA authority. If there is something that they currently have, we are not trying to take anything away. But we are trying to clarify, without going too far, what their authority is and try to sort these things out.

Mr. Coukell, I think you have it; we just have to figure out the combination. You listed in your testimony drawing the line, and you said some of the things we could look at were volume of production, nature of the products, percentage of sales, expiration dates, and interstate commerce.

As you heard previously when I testified, I don't think that interstate commerce alone necessarily does it, because it creates problems in those border areas or where the States are very close to-

gether or smaller. But some combination thereof is probably the answer.

What I would ask each of you to think about—and you can always get back to me later—is, what combination or which number of those factors do you think might be most important in figuring out that trigger to make that distinction? Because I think we all recognize, that is one of the issues we are trying to resolve.

And if we could start with you, Mr. Catizone, if you have thoughts now, or just say, I will send them to you later.

Mr. CATIZONE. Sure. Distinctions we make are: patient-specific, whether it is interstate or intrastate, it is compounding. Non-patient-specific, inter- or intra-, quantity, volume doesn't matter, it is manufacturing.

Mr. GRIFFITH. Manufacturing. OK.

Mr. MILLER. Congressman, our perspective is, you have to be so careful with the issue of volume. It is an easy checkbox, you know, very easy to define. But, unfortunately, in health care, you can't usually rely upon easy—

Mr. GRIFFITH. Let me ask you this, though. If we had volume, plus maybe a percentage of the business crossing State lines, if you threw two or three of them together, do you think that gets us closer to where we need to be?

Mr. MILLER. Yes. And I think you have some precedence already in the Prescription Drug Marketing Act of 1987. That actually sets limits on retail pharmacies of 5 percent of sales to physician offices, hospitals, and clinics before they must register as a wholesaler—precedent.

Mr. GRIFFITH. All right. Let me keep moving down the line so that we don't use up all the time.

Yes, sir?

Mr. COUKELL. Congressman, first, thank you for your leadership on that bill. We were heartened to see the placeholder language and would like to work with you on that.

A couple of points just now. One is, you know, just to emphasize, I think everybody agrees that if somebody is filling a prescription for a patient, that is a traditional pharmacy practice, and nobody is talking about that. So the question is, how much product should people be able to make on spec ahead of time?

And, you know, I mentioned the summit we held with ASHP and AHA. One of the quality experts there said, if somebody is starting with a non-sterile bulk ingredient, they are buying a bottle of methylprednisolone over the Internet and making a sterile product, that ought to be under GMP, no matter what. So his threshold there was zero for that particular type of product. For something that starts with a sterile precursor, you would set a higher threshold.

So I think it would be—I will finish.

Mr. GRIFFITH. Yes, I hate to—we are running out of time.

Mr. COUKELL. I think it would be impossible to say, basically, from a public health point of view, what is the limit at which we would not want people putting product out there.

Mr. GRIFFITH. OK. And if we could, I hate to limit the folks at the other end of the table, but we are running out of time.

Mr. GAUGH. We would leave it at two categories: traditional compounding and——

Mr. GRIFFITH. Manufacturing.

Mr. GAUGH [continuing]. Pharmaceutical manufacturing, yes. Pharmacists are trained to compound. They are not trained to manufacture. It doesn't mean they can't learn, but they are not trained to do that.

Mr. GRIFFITH. Right.

Yes, sir?

Mr. FRANCER. Yes, Congressman Griffith, the touchstone clearly is whether there is a prescription or not. However, the FDA's current guidance in terms of its compliance lists a number of criteria, including compounding finished drugs from bulk active ingredients, using commercial-scale equipment. And the FDA actually has a multiple-factor test that they use.

Mr. GRIFFITH. All right.

Yes, sir?

Mr. THOMPSON. Sir, we appreciate that the bill is a working draft, and we look forward to working with you to clarify key aspects.

You know, the notion of percent of business might be a way to look at it. You know, volume, as mentioned by others, is a moving target. Risk level is a really key one, too. You know, high-risk-level compounding, compounding from API, nonsterile to sterile, is a very important area to focus on

Mr. GRIFFITH. OK.

Mr. THOMPSON. And I will leave it at that, and we will provide more——

Mr. GRIFFITH. I appreciate that. Thank you.

Mr. HOEY. Thank you, Congressman.

A valid prescription, individual valid prescription, is key. That is the starting point and possibly the ending point, as well.

As far as interstate and percentage of prescriptions, percentage of volumes, those are possible, but they can be a slippery slope. And it is hard to have a one-size-fits-all in those categories.

Mr. GRIFFITH. Right.

Thank you all very much. And I look forward to working with all of you in trying to sort this out at some point. We are going to have to make the difficult decision and draw that line somewhere. And I do appreciate it.

I yield back, Mr. Chairman.

Mr. PITTS. The chair thanks the gentleman and now recognizes the ranking member emeritus, Mr. Dingell, for 5 minutes for questions.

Mr. DINGELL. Mr. Chairman, thank you for your courtesy.

One main reason for the NECC outbreak was much confusion regarding FDA's authorities and the proper role of the States. This question is for all of the witnesses, "yes" or "no." Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies, yes or no?

Starting with you, Dr. Hoey.

Mr. HOEY. Yes.

Mr. DINGELL. Next witness?

Mr. THOMPSON. Yes, sir.

Mr. FRANCER. Absolutely, yes.

Mr. GAUGH. Yes.

Mr. DINGELL. Next witness?

Mr. COUKELL. Yes.

Mr. MILLER. Yes.

Mr. CATIZONE. Yes.

Mr. DINGELL. Gentlemen, thank you.

Would you each submit, if you please, to the record how that division of responsibility should be created in the legislation.

Now, Section 503(a) of FDA Modernization Act of 1997 has been subject to court challenges which have limited its effectiveness. Since that time, our medical system has changed drastically.

This question is for Kasey Thompson of the American Society of Health-System Pharmacists.

Do you believe that our healthcare system has come to rely on what you call compounding outsourcers, yes or no?

Mr. THOMPSON. To a greater extent, yes.

Mr. DINGELL. Now, in your testimony, you mention that your members also use compounded sterile preparations which are not available in an appropriate form from a manufacturer. Is that correct, yes or no?

Mr. THOMPSON. Yes.

Mr. DINGELL. Now, can you please submit to the committee for the record a list of examples of these kinds of products?

Mr. THOMPSON. Yes, sir.

Mr. DINGELL. Now, do you believe that these compounding outsourcers should be subject to current good manufacturing practices and risk-based inspections by FDA, yes or no?

Mr. THOMPSON. Yes.

Mr. DINGELL. Do you believe that State boards of pharmacy could adequately regulate these compounding outsourcers, yes or no?

Mr. THOMPSON. No.

Mr. DINGELL. Now, these new compounding outsourcers are now routinely used by hospitals across the country. Any legislation must ensure that there are no unintended consequences which could have a negative impact on patient care.

Now, these questions are for you, Mr. Coukell of Pew. How is it correct that a recent study by the Inspector General at HHS found that 85 percent of hospitals which administer IV drugs purchased some of the products from outside the pharmacies? Is that so, yes or no?

Mr. COUKELL. Yes.

Mr. DINGELL. Now, Mr. Coukell, does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsourcers and our reliance on them, yes or no?

Mr. COUKELL. It does not, not as such.

Mr. DINGELL. Would you submit to us your thoughts on how that matter should be addressed?

And if the other members of the panel would do the same thing, it would be appreciated.

Now, do you believe that simply reinstating Section 503(a) would result in sufficient clarity regarding FDA's authority over compounding pharmacies, yes or no?

Mr. COUKELL. No.

Mr. DINGELL. Would you give us some comments for the purpose of the record on that particular point, if you please?

Now, I want to thank you all.

It is clear that we need to update and to significantly enhance FDA's authority in this area. I know there is bipartisan support for this issue. And we need, I know, to clearly define roles for the States and FDA concerning compounding pharmacies.

This committee has done good bipartisan work on public health in the past, and I believe that we can do it again. And I am looking forward to continue working on this issue with my colleagues on both sides of the aisle.

I want to commend each member of the panel for your excellent testimony. Gentlemen, you have done a superb job, and I want you to know how much I appreciate it.

And to you, Mr. Chairman, I thank you and yield back the balance of my time.

Mr. PITTS. The chair thanks the gentleman and now recognizes the gentlelady from North Carolina, Mrs. Ellmers, for 5 minutes for questions.

Mrs. ELLMERS. Thank you, Mr. Chairman.

Dr. Thompson, a moment ago, one of my colleagues had asked you about whether or not you felt that State boards could actually continue to regulate any of the basically nontraditional compounders. What is your reason? I mean, keeping in mind, of course, safety and sterility and best practices. Do you not feel that they have the capacity to do so?

Mr. THOMPSON. I think it really comes down, ma'am, to resources and expertise. You know, just like pharmacists, we are not inspectors of pharmaceutical manufacturers, and—

Mrs. ELLMERS. Right.

Mr. THOMPSON [continuing]. I don't think State boards tend to have that capacity either.

Mrs. ELLMERS. Right. I guess this gets to the—there again, we seem to get hung up on volume, and, you know, it seems to get back to the same things.

And, you know, to Dr. Woodcock I had posed a question of, if the nontraditional compounder were to be providing to a hospital or an outpatient surgery clinic, where the drugs would be administered under the supervision, obviously, of a physician to a patient within a reasonable timeframe and even possibly with, you know, some certain guidelines, like on a monthly basis, is it that they would be providing that to multiple entities and the volume there would be too much to be enforced?

Mr. THOMPSON. Well, I think the reason we think that some version of CGMPs is important is because it would really get into the specifics of sterility and stability tests in this per FDA and compendial standards. And that would really determine whether it had a 30-, 60-, 90-day, or 12-month beyond-use date associated with it. And that would really determine the storage conditions and when it needs to be administered.

But I think without, you know, a clearer process, whether it is CGMPs or some other process, that you just don't have that assurance in the current environment.

Mrs. ELLMERS. Dr. Gaugh, shouldn't large-scale compounders be required to prove that they can manufacture under GMP conditions before patients are put at risk?

Mr. GAUGH. Yes, they should be.

Mrs. ELLMERS. OK. In your testimony, you write about the importance of the drug manufacturing control process. Can you outline why this process between the FDA and applicant is critical to ensure the safety and efficacy of the product that will be ultimately marketed?

Mr. GAUGH. Again, it is all about the CGMP requirements that exist between the FDA and the manufacturer. And those requirements don't exist between the State boards of pharmacy and the compounders to the same degree and the same level. And, as Dr. Thompson stated, they are not typically trained to inspect to that, whereas the FDA is. So it needs to fall into that same category.

Mrs. ELLMERS. So can you explain, the similar scope of risk between ANDA holders manufacturing drugs and large-scale compounders in relation to, you know, explaining and creating two regulatory regimes for large-scale compounders and manufacturers. So I am concerned I don't understand that process.

Mr. GAUGH. So if I understand the question correctly, when you look at what the ANDA and the NDA holders are required to do, they have specifications they must meet around the potency of the product, around potential impurities and impurity growth around microbe growth. That doesn't exist currently in the compounding structure, in the compounding review. It would under CGMP requirements, but it doesn't under current requirements.

Mrs. ELLMERS. So it would under—OK, again—

Mr. GAUGH. It could, I should say.

Mrs. ELLMERS. It could.

Mr. GAUGH. Yes.

Mrs. ELLMERS. But it does not at this time?

Mr. GAUGH. It does not.

Mrs. ELLMERS. OK. And so, again, expanding on that, do you see risk in creating two more regulatory regimes? I mean, essentially, would there be two separate regulatory processes here or—

Mr. GAUGH. In our opinion, that would be creating two different regulatory processes at the FDA, if they were the ones controlling this. They would be controlling a manufacturer process for CGMP—

Mrs. ELLMERS. For compounding and manufacturing.

Mr. GAUGH [continuing]. To be different. And we don't see the manufacturing processes being different, so, therefore, the structure of control should not be different.

Mrs. ELLMERS. OK.

I only have about 40 seconds left.

To Dr. Miller, again, getting back to just the importance of the physician role in this, why is the anticipatory compounding important to physicians?

Mr. MILLER. Having medicine available. When the patient comes to you, you don't want to send that patient—give them a piece of

paper, send them down to the compounding pharmacy, where it may take 2 to 14 days to prepare and test that, then come back to be treated.

Mrs. ELLMERS. Yes.

Mr. MILLER. Physicians want to treat you today. Pharmacists want to treat you today. We have to be able to prepare medicines in advance.

Mrs. ELLMERS. Very good.

And I see that my time has run out, so thank you, Mr. Chairman.

Thank you to the panel.

Mr. PITTS. The chair thanks the gentlelady and now recognizes the gentlelady from the Virgin Islands, Dr. Christensen, for 5 minutes for questions.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman.

Mr. Catizone, in your testimony, one of the limitations you suggest on compounding in advance of a prescription for traditional compounders is that the total quantity provided to a healthcare provider not exceed a 10-day patient supply.

I am interested in NABP's views on an alternative or additional approach to a limitation on compounding in advance of or without a prescription, of something like a 10- or 14-day expiration date from time of manufacture.

As I understand it, one of the aspects of traditional pharmacy compounding that contributes to safety is that it ordinarily is performed for an individual patient at a time the patient needs and will use the drug. One of the problems with allowing traditional compounders to make drugs in advance or without a prescription is that the drugs can be made in unlimited quantities and allowed to sit on a shelf, either in the compounder's warehouse or in the healthcare provider's offices, for extended periods of time. During that time, any bacterial, fungal, or other biological contaminants have time to grow and make the product more dangerous.

A relatively short expiration date from the time of manufacture would presumably limit the amount of drug that would be compounded in advance of an order, limit the size of orders that healthcare providers would request, and limit the amount of time any contaminants could grow.

So what are your thoughts about such an approach?

Mr. CATIZONE. Under the limitations we propose, there were two factors: one, the patient supply, as well as the total quantity the pharmacy would provide.

The 10- to 14-day expiration date is another variable that we could support, provided that that expiration date coincides with what the beyond-use dates are with the product so that we didn't put a 10-day or a 14-day expiration when the product was only good for 2 or 3 days. So coinciding those two factors makes that another very viable factor to look at in this process.

Mrs. CHRISTENSEN. Does anyone else have an opinion or want to comment on it?

Mr. HOEY. The USP requirement for a USP 797 standards would also help to address some of the issues that you are talking about.

I would also mention an example of the importance of anticipatory compounding. There was a situation where there was a

shortage of injectable atropine for crash carts, for emergency crash carts. And because that drug wasn't available, a compounding pharmacy was able to make that. Well, if a patient is crashing, you don't want to have to write a prescription at that moment while your patient is coding. When that patient has had the proper treatment from the nurses and the physicians and the pharmacists, then you can write the prescription. But not having that prescription available at the time could cause someone to die.

So that is a situation where there is a shortage of the drug, and because compounding pharmacists have made that drug, it is available when the patient needs it immediately.

Mrs. CHRISTENSEN. Yes. I think in a situation like that, as I understood it from Dr. Woodcock's testimony, because it is an emergency drug not available, that that would be something that they would allow.

Mr. HOEY. And there would have to be a stock on those crash carts that are on—

Mrs. CHRISTENSEN. Absolutely.

Mr. HOEY [continuing]. Certain floors in the hospital.

Mrs. CHRISTENSEN. Absolutely.

Mr. HOEY. And it wouldn't be just that drug. There would be several drugs that are on those crash carts.

Mrs. CHRISTENSEN. If there are no other comments, Mr. Chairman, I don't have another question.

Mr. PITTS. The chair thanks the gentlelady and now recognizes the gentleman from Pennsylvania, Dr. Murphy, for 5 minutes for questions.

Mr. MURPHY. Thank you, Mr. Chairman. Thank the panel.

By the way, Mr. Chairman, I have an opening statement I would like to submit for the record, too.

[The prepared statement of Mr. Murphy follows:]

PREPARED STATEMENT OF HON. TIM MURPHY

Thank you, Chairman Pitts, for holding this hearing to further the discussion about FDA's authority over drug compounding.

Soon after the fungal meningitis outbreak began in the fall of 2012, the Oversight and Investigations Subcommittee initiated a thorough investigation to determine whether this tragic outbreak—which has now claimed the lives of over 60 people and sickened nearly 750 others—could have been prevented.

The Subcommittee found that the New England Compounding Center was not operating in the shadows; in fact, they were operating right under FDA's investigative nose for a decade. Our investigation highlighted several opportunities where the agency confronted a choice in dealing with NECC and its sister company, Ameridose. FDA repeatedly decided not to act. Furthermore, as FDA has recently confirmed to the Committee, not a single complaint the agency had independently received about these companies over the past decade was forwarded to the state pharmacy board.

It is very hard to legislate cultural change into a large federal agency. However, Mr. Griffith's discussion draft makes important changes to address the breakdowns that occurred at FDA in the NECC case. His legislation is grounded in the facts uncovered by our investigation and makes it clear when FDA can—and must—put patients before process. I commend him for his efforts, and look forward to continue working with my colleagues to reform drug compounding rules so patients receive safe and effective medications.

Mr. MURPHY. All right. I am also the chairman of Oversight and Investigations, and we had a number of hearings on this to try and

get the FDA to give us a straight answer. We didn't get it from Dr. Hamburg. I am going to try and ask you folks.

If the FDA has reason to believe that a compounding pharmacist is acting like a manufacturer, do you believe the FDA should have the authority to inspect a facility to the extent necessary to determine if that is the case?

Let's go down the panel. Dr. Hoey?

Mr. HOEY. In cooperation with the State board of pharmacy, yes.

Mr. MURPHY. Dr. Thompson?

Mr. THOMPSON. If they are truly acting as a manufacturer, yes.

Mr. MURPHY. Mr. Francer?

Mr. FRANCER. Yes.

Mr. GAUGH. Yes.

Mr. MURPHY. Mr. Coukell?

Mr. COUKELL. Yes, but of course they have to know that that facility is out there.

Mr. MURPHY. OK.

Dr. Miller?

Mr. MILLER. Yes. And it already has that authority under 704(a).

Mr. MURPHY. Thank you.

Mr. CATIZONE. Yes.

Mr. MURPHY. OK.

So when we had our hearing before, I could not get an answer from Dr. Hamburg on that, because what it appeared was that they had, like, a 1-year moratorium against doing inspections without cause, it was said, that had made the medication that infected so many with meningitis.

And I asked several times, six or seven times, about this, and her responses were—I said, “For example, in terms of dealing with the definition of a compounding pharmacy, who is responsible for that?” She said, “Well, it is not the FDA, it is Congress.” I said, “But who keeps that definition?” She said, “Our chief counsel.” “So have you reviewed this definition with your chief counsel?” She said, “I think everyone agrees.” And I said, “I didn't ask you if you agree.” She said, “The law is clear.” And I said, “I want to know, have you reviewed with someone the definition of 'compounding' versus 'drug manufacturing'? Have you reviewed that with someone? When did that take place?” She said, “You know, we have had a lot of discussions.” I frustratingly said, “So has someone reviewed with you the definition of 'manufacturer' versus 'compounding'?” She says, “You know, that is unfortunate. It is not clear.”

It went on. I said, “Well, wait a minute. If you are telling me you don't have the authority to inspect based upon whether or not someone is a compounder versus a manufacturer, someone must be advising the FDA on where you have jurisdiction and where you do not.” At that point, she said it was too complex and we couldn't understand.

Now, all of you answered that question pretty straightforward. You thought that there was authority with regard to this. But this is a key part of this issue and one that I want to find out. I mean, clearly, if we need more jurisdiction, we need to review that, in terms of the safety of patients and make sure people understand what is to be done here. But the way you all responded to me, it sounds like it already is there.

So I am going to go into a little more detail with this. Do you all believe, yes or no, is there a clear definition of “manufacturing” that defines when the FDA can come in and not?

Dr. Hoey?

Mr. HOEY. Yes, there is a clear definition of “manufacturing.” And the FDA, as my colleague from PhRMA mentioned, the FDA does a good job of monitoring CGMP, and they do a good job of regulating manufacturers.

Mr. MURPHY. Dr. Thompson?

Mr. THOMPSON. I think there is, yes. But these large-scale entities aren’t behaving like manufacturers that have an NDA or an ANDA.

Mr. MURPHY. When you say a large-scale entity, meaning what?

Mr. THOMPSON. Well, like the compounding-manufacturer-type entities. I mean, they are really big compounding pharmacies. They are registered as pharmacies in all 50 States. There are non-resident license agreements.

Mr. MURPHY. OK, so this is not a mom-and-pop. This is someone who makes a lot of—

Mr. THOMPSON. Yes, but they are essentially compounding at a very—

Mr. MURPHY. On a large scale.

Mr. THOMPSON [continuing]. Large scale. They are not, often, commercially available products, unless there is a shortage, that are customized dosage forms. They are just doing—

Mr. MURPHY. I see. And the FDA has the authority to go into those?

Mr. THOMPSON. I think they fall under the jurisdiction of the State boards under the current construct. And I think that is concerning for us, because these look more like manufacturing entities, but they are not. And I don’t think the State boards have the capability to regulate them.

Mr. MURPHY. Mr. Francer?

Mr. FRANCER. Congressman, I believe the FDA knows manufacturing when the agency sees it and that, as a matter of patient safety, they should be using their authority to the maximum extent possible.

Mr. MURPHY. Dr. Gaugh?

Mr. GAUGH. Yes. Once identified, I think they have the authority to step in.

Mr. MURPHY. Mr. Coukell?

Mr. COUKELL. I think the authority to investigate after a problem has been identified is not the same as having the authority and the tools to proactively ensure quality. And that is what we are missing.

Mr. MURPHY. Yes, what we found in this case with NECC is that they complaints from everybody—patients, doctors, whistleblowers—who were all saying, there is a problem here, and the FDA didn’t act. So that is a question, and I still think that is one of my concerns with this whole issue. Is it that we need a bill or do we need an FDA that takes action within that?

Dr. Miller?

Mr. MILLER. I am going to answer backwards.

Mr. MURPHY. Yes.

Mr. MILLER. Yes, we believe they have adequate authority and a definition.

However, the approach and the answers that you received from Commissioner Hamburg implies that any one of us could go into our garage, start an illegal drug company, put that medication out into the marketplace, and the FDA would not be able to shut me down? If that is indeed the case and that is the confusion, when we address this legislation, we have to make it very clear that illegal, inappropriate manufacturing falls under the jurisdictional authority of the FDA.

Mr. MURPHY. Thank you.

Mr. CATIZONE. There is not a clear definition.

Mr. MURPHY. I see my time is up, and I am still seeking an answer.

Thank you very much.

Mr. PITTS. The chair thanks the gentleman.

That concludes the questions from the Members who are here. We will have follow-up questions. I am sure other Members will have questions. We ask that you please respond promptly when we submit them to you.

I will remind Members that they have 10 business days to submit questions for the record. And so Members should submit their questions by the close of business on Tuesday, July 30th.

Superb hearing. Excellent testimony. Thank you all so much for coming.

Without objection, the subcommittee is adjourned.

[Whereupon, at 5:45 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

PREPARED STATEMENT OF HON. FRED UPTON

This legislative hearing is the product of the thorough, thoughtful, and bipartisan investigation that the committee launched in the wake of last fall's tragic meningitis outbreak. We were deliberate in our efforts as we wanted to know what went wrong and why before the committee acted legislatively. Sadly, Michigan has been hit hardest by the outbreak—according to CDC data last updated July 1, 2013, 264 of the 749 illnesses caused by the outbreak were in Michigan and we have endured 17 of the 61 fatalities, including three from my own district.

During our committee's investigation, under the leadership of Oversight and Investigations Subcommittee Chairman Tim Murphy, we found that the meningitis outbreak and the loss of innocent lives could have been prevented. The New England Compounding Center was operating in an unacceptable and unlawful manner for years. Yet, it took this outbreak and its tragic consequences for the Food and Drug Administration (FDA) to act. Although the facts demonstrate that the FDA had the authority to regulate the bad actors who harmed patients with unsafe products, we believe that clarifying FDA's regulatory authority in this area through legislation is a prudent step toward improving the safety of all Americans.

In May, this subcommittee held a hearing on the drug compounding industry to understand its evolution and the current role it plays in our health care system. We learned that compounding is an integral part of our health care system that helps patients receive the treatments necessary for their unique medical needs. As we look to legislate in this area, we want to ensure that patients can continue to receive compounded drugs that are safe. I believe that everyone here today shares that goal.

We also want to ensure that bad actors can no longer use the good name of pharmacies to hide activity that is essentially large-scale drug manufacturing. The FDA gold standard for approval should give patients the assurance that the drugs they use are safe and effective. Activities akin to large-scale manufacturing must be regulated as such in order to uphold the integrity of our nation's drug supply.

Our hearing today is a result of thorough and collaborative investigative and policy work. While all of the bills before us today include ideas that we should consider carefully, I would like to thank Morgan Griffith for his dedication and leadership throughout both the committee's investigative and legislative process. The Griffith discussion draft before us today includes key provisions that serve the important goals of clarifying FDA's authority and protecting the role of traditional compounding. As we continue to work in a bipartisan manner, it is my belief that we will find common ground to advance legislation that achieves these goals.

Thank you, Mr. Chairman. I yield my remaining time to



EXPRESS SCRIPTS®

July 16, 2013

The Honorable Morgan Griffith
U.S. House of Representatives
Washington, DC 20515

Dear Congressman Griffith:

Express Scripts would like to thank you for your hard work in drafting the Compounding Clarity Act of 2013. Express Scripts is the nation's largest pharmacy benefit manager (PBM). We administer the prescription drug benefits on behalf our clients – employers, health plans, unions and government health programs — for approximately 100 million Americans. Headquartered in St. Louis, we provide integrated pharmacy benefit management services including specialty pharmacy and patient-care services.

Through our specialty pharmacies, Express Scripts does engage in a traditional pharmacy compounding. For example, we compound sterile saline cassettes for Remodulin® for patients with a certain form of pulmonary arterial hypertension (PAH). Patients on this therapy—generally the most progressively ill patients with PAH—are required to have a continuous course of therapy for the remainder of their lives. Going without therapy for even a few hours is fatal. In order for these patients to process the drug, Remodulin® needs to be diluted with a small amount of salt water via these saline cassettes. This product is not commercially available from any manufacturer—nor is it likely to be given the extremely small patient population. Essentially what Express Scripts does is purchase commercially available sterile saline and subdivide it into approximately 150 cassettes. Every batch is sent out to an independent lab for testing per United States Pharmacopeia (USP) 797 standards for potency, purity, and sterility. All shipments are quarantined until we receive the results. When they come back they have a “beyond use” date and are tracked exactly back to the original saline product by lot number and put on the patient prescription all before being shipped out the door via the mail. We obviously know how many PAH patients we have and roughly how many saline cassettes they will need. We do this sort of “anticipatory compounding” for quality control reasons and as a patient benefit to keep them on continuous therapy. This allows us to ship 14-30 cassettes (depending on the patient's therapy) with a month's supply of drug. And, the patient doesn't run the risk (which could be fatal) of being out of cassettes or having to obtain them every week.

We believe your bill, as currently drafted, elevates the practice of pharmacy compounding by applying the USP 797 standard to all sterile compounding while preserving the traditional role pharmacies have had in providing these preparations for critical patient populations. It also properly recognizes the distinction between pharmacy compounding and drug manufacturing.

We have concerns with S. 959 as passed by the U.S. Senate Committee on Health, Education, Labor and Pensions (HELP). While well meaning, this legislation would subject the sort of

compounding that Express Scripts' engages in to current good manufacturing practices (cGMP) because we do anticipatorily compound (albeit for a known patient population) and we deliver our preparations as prescribed to patients through the mail. We have assessed that it would be extraordinarily difficult, if not impossible, to convert our compounding pharmacy into a manufacturing facility for these small groups of patients (e.g. in this case, approximately 35 nationwide.) It actually would make more sense for the patients to self-compound their saline cartridges—a result we believe would not be in the patients' best interest.

As drafted, the Compounding Clarity Act of 2013 would strike the right balance between preserving traditional pharmacy compounding, while improving compounding standards and increasing coordination between the various state boards of pharmacies and the U.S. Food and Drug Administration. We thank you for your efforts and look forward to working with you on its passage.

Sincerely,

Mary Rosado
Vice President
Express Scripts



Statement
Of
The National Association of Chain Drug Stores

For:

U.S. House of Representatives
Committee on Energy and Commerce
Subcommittee on Health

Hearing on:

“Reforming the Drug Compounding
Regulatory Framework”

July 16, 2013
3:00 p.m.

2123 Rayburn House Office Building

National Association of Chain Drug Stores (NACDS)
1776 Wilson Blvd., Suite 200
Arlington, VA 22209
703-549-3001
www.nacds.org

The National Association of Chain Drug Stores (NACDS) thanks Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee on Health for consideration of our statement for the hearing “Reforming the Drug Compounding Regulatory Framework.” We commend the Committee for its ongoing efforts to adequately evaluate and, where necessary, address issues related to the compounding of prescription drugs. NACDS welcomes the opportunity to work with you on this important task to ensure that policies are in place that facilitate access to safe and effective compounded prescription drugs.

NACDS represents traditional drug stores, supermarkets, and mass merchants with pharmacies – from regional chains with four stores to national companies. Chains operate more than 41,000 pharmacies and employ more than 3.8 million employees, including 132,000 pharmacists. They fill over 2.7 billion prescriptions annually, which is more than 72 percent of annual prescriptions in the United States. The total economic impact of all retail stores with pharmacies transcends their over \$1 trillion in annual sales. Every \$1 spent in these stores creates a ripple effect of \$1.81 in other industries, for a total economic impact of \$1.81 trillion, equal to 12 percent of GDP. For more information about NACDS, visit www.NACDS.org.

Introduction

As we conveyed in a previously submitted statement to the Committee in May 2013, NACDS supports the mission and work of FDA in ensuring that Americans receive only safe and effective prescription drugs. Safeguarding the health and welfare of our patients remains our highest priority. Pharmacist compounding services are the only source of critical medications for millions of patients who each have their own unique health care needs. For these patients, there are no commercially-manufactured preparations available. Accordingly, we agree with FDA that prescription drug compounding services are a valuable and important part of our nation’s healthcare system.

Background on Compounding

Since the early days of the pharmacy profession, prescription drug compounding has been a traditional function of the practice of pharmacy. Throughout the years, pharmacists have continued this core practice, compounding medications based on prescription orders for individual patients whose needs cannot otherwise be met with commercially available products. Prescription drug compounding addresses critical medical needs for many such patients.

State boards of pharmacy regulate both practicing pharmacists who engage in compounding and the pharmacy facilities wherein they practice. State boards of pharmacy require that pharmacists be properly trained to prepare compounded medications and test pharmacists on this competency. Additionally, state boards of pharmacy license pharmacies after ensuring that, among other things, they have the proper tools and equipment to compound prescription drug medications.

The state pharmacy practice acts enforced by boards of pharmacy consistently define the activities that constitute “compounding.” Generally, the practice involves the mixing of two or more drug substances together to deliver to the patient a product that is not commercially available. Most retail pharmacies engage in the compounding of skin creams, lotions, ointments, liquids, or suppositories to meet the needs of individual patients who require medications that are not otherwise commercially available.

Some chain pharmacies may have a local or regional central compounding facility that they use to compound frequently-ordered products that are not commercially available, which are then distributed to individual retail stores in the chain. These compounded products are made in anticipation of prescriptions for these products based on the prescribing patterns of physicians.

NACDS Supports Regulating the Practice of Compounding in a Manner that Preserves State Board Authority and Promotes State and Federal Collaboration

NACDS believes that state boards of pharmacy should retain sole jurisdiction over traditional prescription drug compounding. State boards of pharmacy have the experience and expertise to

continue to regulate this integral function of pharmacy practice. Although it is appropriate for FDA to regulate the manufacturing of prescription drugs, FDA should not be granted authority over traditional pharmacy functions. FDA would not have the resources, ability or expertise to regulate pharmacies and the practice of pharmacy. Moreover, concurrent state and federal jurisdiction over pharmacies would cause unnecessary confusion for FDA, state boards of pharmacy, and pharmacies. All would be unsure as to where federal authority ends and state authority begins. Thus, we support legislative initiatives to maintain the authority of state boards of pharmacy to oversee and regulate traditional compounding practices while appropriately focusing FDA's authority on manufacturing.

NACDS recognizes the importance of collaboration between FDA and the state boards of pharmacy to investigate any questionable practices so that prescription drug compounding is regulated in the best interests of patients. Despite best efforts, there still may be entities that seek to circumvent patient safety measures as well as federal and state regulation. To prevent future tragedies, closer collaboration between FDA and state pharmacy regulators would serve to root out rogue entities that seek to use a state pharmacy license as a shield from federal oversight. To this end, we support legislative initiatives to establish a reporting tool for state boards of pharmacy to identify compounding pharmacies that may be in violation of accepted compounding practices and/or are operating as a manufacturer. This would provide FDA with targeted information that would prompt the agency to focus their inspection activities where they are most needed.

Important to Maintain Pharmacists' Ability to Provide Traditional Prescription Drug Compounding Services

Prescription drug compounding practices enable pharmacists to meet the medication needs of their patients that cannot be met with commercially available products. There are numerous circumstances in which it is both appropriate and necessary for pharmacists to compound medications. For example, chain pharmacists helped to meet the need for liquid Tamiflu during the 2009 H1N1 flu outbreak through their ability to compound the liquid product from Tamiflu capsules – and at the request of FDA. In other cases, a pharmacist may be called on to

compound a liquid form of a medication for a patient battling cancer, when that patient is not able to swallow the pill form of the medication. So that patients have access to the important compounding services provided by pharmacists, we support legislative initiatives that recognize and maintain the ability of pharmacists to provide these types of traditional prescription drug compounding services. This includes compounding of commercially available products where the prescriber determines the variation will have a clinical difference for a particular patient; and compounding of commercially available products that are in shortage as identified on a public or private national or regional shortage list. Legislative initiatives must ensure that pharmacists are allowed to continue to provide compounded prescription drug medications in these circumstances to meet critical patient needs.

Conclusion

NACDS thanks the Committee for consideration of our comments. We look forward to continuing to work with policy makers and stakeholders on these important issues.



1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

The Honorable Joseph Pitts
Chairman, Health Subcommittee
Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Frank Pallone
Ranking Member, Health Subcommittee
Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

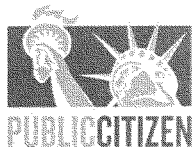
July 15, 2013

Dear Chairman Pitts and Ranking Member Pallone:

Enclosed please find a written statement from Public Citizen regarding three pending pieces of legislation on pharmacy compounding: the Pharmaceutical Compounding Quality and Accountability Act (S. 959), Verifying Authority and Legality in Drug (VALID) Compounding Act (H.R. 2186), and the draft bill recently proposed by Congressman Morgan Griffith. We ask that this statement be submitted for the record as part of the testimony at the hearing entitled, "Reforming the Drug Compounding Regulatory Framework" on July 16, 2013. Thank you for your attention to this matter.

Sincerely,

David Sterrett
Health Care Counsel



1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

Public Citizen's Comments Regarding Pending Legislative Proposals on Compounding Pharmacies

July 12, 2013

Thank you for the opportunity to provide comments regarding three pending pieces of legislation on pharmacy compounding: the Pharmaceutical Compounding Quality and Accountability Act (S. 959), Verifying Authority and Legality in Drug (VALID) Compounding Act (H.R. 2186), and the draft bill recently proposed by Congressman Morgan Griffith.

Public Citizen, a consumer advocacy organization with more than 300,000 members and supporters nationwide, wishes to express our grave concerns with all three pieces of proposed legislation. There may be significant differences between these three proposals, but all of them put patients at risk by permitting compounding pharmacies to engage in drug manufacturing activity without seeking a new drug approval from the Food and Drug Administration (FDA) or complying with important federal drug labeling requirements.

We believe there is a legitimate public health role for traditional compounding, which involves the individualized tailoring of medicines in response to a physician's prescription, for a patient with unique medical needs that cannot be met by an FDA-approved product. This activity is appropriately regulated by state boards of pharmacy, with a much more limited role for federal oversight. However, when a company calling itself a "compounding pharmacy" produces standardized drug products on a large scale without first obtaining an individualized patient-specific prescription, it is engaged in drug manufacturing activity that exceeds the scope of traditional compounding. Any entity that engages in drug manufacturing should be required to obtain a new drug approval from the FDA and demonstrate compliance with all current federal requirements designed to ensure the safety, efficacy, and quality of manufactured drugs.

Although the FDA has the authority to prevent much of this illegal drug manufacturing under current law, its existing authority also could be strengthened to reduce the costs of enforcement and limit abuses by pharmacies who seek to flaunt current federal requirements and manufacture drugs without FDA approval. None of the three legislative proposals being discussed by the House accomplish this important goal of strengthening the FDA's authority to stop the manufacture of unapproved drugs.

We have previously expressed our concern to the Senate Health, Education, Labor, and Pensions Committee that S. 959 creates a second, substandard tier of drug manufacturers, confusingly called "compounding manufacturers." These compounding manufacturers would not be required to seek new drug approval by the FDA or comply with important federal labeling requirements

for new drugs.¹ We believe that any such tier system is unacceptable: All drug manufacturers should be held to the same standards.

Although the draft bill proposed by Congressman Griffith does not expressly create a second category of compounding manufacturers, this proposal will have essentially the same effect by permitting compounding pharmacies to engage in drug manufacturing activity (creating standardized, mass-produced products rather than individually tailored drugs) without seeking a new drug approval or complying with all federal drug labeling requirements. The Griffith proposal does this both by maintaining an “advanced compounding” provision that has previously been abused by compounders seeking to evade FDA authority, and by adopting an additional broad new exception that permits unlimited non-patient-specific purchasing by health care providers who administer the products in a physician’s office, hospital, or other health care setting. This provision is particularly dangerous because many high-risk sterile drugs are administered in health care settings.

The VALID Compounding Act, though structured differently than the other two proposals, also includes a flawed provision that will allow pharmacy compounders to scale up their operations and engage in drug manufacturing activities without seeking new drug approval. The bill does this by permitting a pharmacy to compound without receiving an individual patient-specific prescription as long as the pharmacy registers with the FDA and follows other conditions and limitations that the FDA will specify. We do not believe that new conditions and limitations are appropriate for these entities. Instead, we believe that all companies that wish to engage in drug manufacturing should be required to obtain new drug approval.

Public Citizen believes that better legislation is possible. We urge you to reject all three current proposals and instead adopt a bill that would:

- Draw a clear line between drug manufacturing and compounding, with no loophole for “advanced compounding” or other forms of large-scale production of unapproved drugs, to ensure that all manufactured drugs are subject to the same requirements;
- Strengthen the FDA’s authority to police the line between traditional compounding and drug manufacturing by requiring compounders to register with the FDA and granting the FDA authority to inspect traditional pharmacies to ensure that they are not engaged in drug manufacturing;
- Prevent dangerous compounding of certain high-risk drugs by giving the FDA authority to identify dosage forms and active ingredients that cannot be compounded, including complex dosage forms, drugs that have been withdrawn for reasons of safety and efficacy, and active ingredients that have never been FDA-approved due to concerns about safety and efficacy; and
- Require clear, standardized warning labels to communicate to providers and patients who purchase compounded products that these products are not FDA-approved and the safety, efficacy, and accuracy of the product’s labeling have not been assessed by the FDA.

¹ Public Citizen’s Comments to the Senate HELP Committee Draft Proposal for Regulatory Oversight of Compounding Pharmacies. May 3, 2013. <http://www.citizen.org/hrg2121>. Accessed July 12, 2013.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3841

August 13, 2013

Dr. Janet Woodcock
Director
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Woodcock:

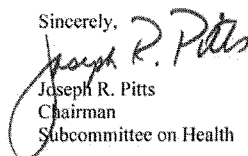
Thank you for appearing before the Subcommittee on Health on Tuesday, July 16, 2013, to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework."

During the hearing, Members asked you to provide additional information for the record, and those requests are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose request you are addressing, (2) the complete text of the request you are addressing in bold, and (3) your response to that request in plain text.

To facilitate the printing of the hearing record, please respond to these questions and requests by the close of business on Tuesday, August 27, 2013. Your responses should be mailed to Sydne Harwick, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Sydne.Harwick@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachment



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

FEB 18 2014

Dear Mr. Chairman:

Thank you for providing the Food and Drug Administration (FDA or the Agency) with the opportunity to testify at the July 16, 2013, hearing before the Subcommittee on Health, Committee on Energy and Commerce, entitled "Reforming the Drug Compounding Regulatory Framework." This letter is a response for the record to questions posed by certain Members of the Committee, which we received on August 13, 2013.

If you have further questions, please let us know.

Sincerely,

A handwritten signature in black ink, appearing to read "Sally Howard".

Sally Howard
Deputy Commissioner
Policy, Planning, and Legislation

Enclosure

cc: The Honorable Frank Pallone, Jr.
Ranking Member
Subcommittee on Health

Page 2 - The Honorable Joseph R. Pitts

We have restated each Member's questions below in bold, followed by our responses.

The Honorable John D. Dingell

1. **What authority does the FDA need to require all compounding pharmacies to register with the Agency?**

Please see the enclosed document (*July 16th, 2013 Statement of Janet Woodcock Before the Subcommittee on Health, Committee on Energy and Commerce*), provided to respond to the following Questions 1-6, and 8, from Mr. Dingell, on necessary authorities.

2. **What authority does the FDA need to require all compounding pharmacies to report adverse events?**
3. **What authority does the FDA need to require all compounding pharmacies to follow good manufacturing practices?**
4. **Does FDA believe nontraditional compounders should be subject to appropriate good manufacturing practices like manufacturers? Please elaborate.**
5. **Does FDA believe a risk-based inspection schedule is appropriate for non-traditional compounders? Please elaborate.**
6. **What authority does the FDA need to see all records when inspecting any compounding pharmacy?**
7. **Has FDA faced litigation regarding its ability to inspect records in pharmacies? Please elaborate.**

The following list includes the most significant legal challenges to FDA's authority over compounding since the early 1990s and the parties involved. This list is not exhaustive.

Professionals & Patients for Customized Care (P2C2) v. Shalala, 56 F.3d 592 (5th Cir. 1995)

- According to the International Association of Compounding Pharmacists' (IACP) website (<http://www.iacprx.org/>), P2C2 represents 164,000 patients and practitioners.

- P2C2 challenged FDA's Compliance Policy Guide on compounding soon after it was issued in 1992 on the basis that it violated the Administrative Procedure Act's notice-and-comment rulemaking requirements.

Thompson v. Western States Medical Center, 535 U.S. 357 (2002)

- Plaintiffs were a group of seven pharmacies: Western States Medical Center Pharmacy; Women's International Pharmacy; Health Pharmacy; College Pharmacy; Wedgewood Village Pharmacy; ApothéCure, Inc.; and Lakeside Pharmacy.
- Plaintiffs challenged the constitutionality of the solicitation and advertising provisions in section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act).

Wedgewood Village Pharmacy v. U.S., 421 F.3d 263 (3d Cir. 2005)

- On March 10, 2003, FDA sought an administrative warrant from a Federal court to inspect Wedgewood's facilities and to access certain records. Wedgewood moved to quash the warrant, arguing that the FD&C Act provides state-licensed pharmacies a total exemption from FDA inspection.

Medical Center Pharmacy v. Mukasey, 536 F.3d 383 (5th Cir. 2008)

- Plaintiffs were a group of 10 pharmacies: Medical Center Pharmacy; Applied Pharmacy; College Pharmacy; Med Shop Total Care Pharmacy; Pet Health Pharmacy Incorporated; Plum Creek Pharmaceuticals Incorporated; Premier Pharmacy; University Compounding Pharmacy; Veterinary Pharmacies of America; Women's International Pharmacy.
- Plaintiffs sought declaratory and injunctive relief against FDA, arguing, among other things, that the Agency: 1) cannot regulate compounded drugs as "new drugs" within the meaning of the FD&C Act, and 2) cannot inspect the records of the plaintiff pharmacies because of their claim that they are exempt from a records inspection under section 704(a)(2)(A) of the Act.

U.S. v. Franck's Lab, 816 F. Supp. 2d 1209 (M.D. Fla. 2011)

- After compounded drugs from Franck's Lab caused the death of 21 polo ponies, FDA sought an injunction to prevent the pharmacy from compounding animal drugs using bulk drug substances. Franck's Lab contested FDA's jurisdiction over its animal drug compounding practices.

FDA's authority to inspect has also been challenged on several occasions. In a sample of 226 pharmacy inspections¹ between 2002 and 2012 that FDA has conducted on practices related to pharmacy compounding of human and veterinary drugs, pharmacies have refused at least one FDA request in more than 25 percent of inspections. For example, 4 percent of firms refused FDA entry into their facility, and of those firms that did grant entry, 12 percent refused FDA access to records (e.g., shipping records, dispensing records, product formulas, and/or standard operating

¹These 226 inspections represent the number of inspections recorded under the human and veterinary pharmacy compounding Program Assignment Codes (PAC Code) between 2002 and September 25, 2012, which FDA has conducted of pharmacies based on practices related to pharmacy compounding of human and veterinary drugs. Not all compounding pharmacy inspections were recorded under this PAC Code, in part, because some firms engage in multiple types of activities. In addition, some inspectional activities may have been coded as "investigations" rather than "inspections" and, therefore, are not captured in this figure. Thus, we know that FDA conducted additional inspections of firms that could be classified as compounding pharmacies that are not accurately reflected in our databases.

procedures). Other refusals include the ability to observe drug production processes, collect samples, access portions of the facility, or take photographs.

FDA encountered refusals of at least one FDA request during inspections of the following compounding pharmacies between 2002 and September 25, 2012. This may not be an exhaustive list:

2002

- Lee and Company, Inc. dba Lee Pharmacy, Fort Smith, AR (July 2002)
- Med-Mart Pacific Pulmonary Services Pharmacy, Bakersfield, CA (November 2002)

2003

- Plum Creek Pharmaceuticals, Inc., Amarillo, TX (February 2003)
- Med 4 Home Pharmacy, Kansas City, MO (March 2003)
- Med-Mart Pacific Pulmonary Services Pharmacy, Bakersfield, CA (May 2003)
- Unique Pharmaceutical, Ltd., Temple, TX (August 2003)
- Monument Pharmaceutical Co., Inc., Winchester, VA (September 2003)

2004

- Keyes Drug, Newton, MA (April 2004)
- Reliant Pharmacy, Southaven, MS (May 2004)
- Reliant Pharmacy, Southaven, MS (June 2004)
- Essential Pharmacy Compounding, Omaha, NE (August 2004)
- Pet Script, Inc., Paris, TX (August 2004)
- University Rx Specialties, Inc. (September 2004)
- ApothéCure, Inc., Dallas, TX (September 2004)
- Kubat Custom Healthcare, Omaha, NE (September 2004)

2005

- PharMEDium Services, Sugar Land, TX (March 2005)
- Pulmo-Dose Inc., Murray, KY (August 2005)
- Civic Center Pharmacy, Scottsdale, AZ (October 2005)
- Pharmacy Creations, Randolph, NJ (October 2005)
- Wedgewood Village Pharmacy, Swedesboro, NJ (October 2005)
- Alchemist Shoppe, P.C., Denville, NJ (November 2005)
- Spoonamore Drug Co., Inc., Louisville, KY (December 2005)

2006

- Pharmacy Creations, Randolph, NJ (February 2006)
- D.R. Pharmacy, Inc., Midland, TX (March 2006)
- Oakdell Pharmacy, Inc., San Antonio, TX (April 2006)
- Hopewell Pharmacy and Compounding Center, Hopewell, NJ (October 2006)

2007

- Newman Inc. dba Medi-Stat, Mobile, AL (February 2007)
- ApothéCure, Inc., Dallas, TX (May 2007)
- Advanced Physician Solutions, Inc., North Hollywood, CA (July 2007)
- Leiter's Pharmacy, San Jose, CA (September 2007)
- Calvert-Gamble Pharmacy, Inc. dba Southern Meds Joint Venture, Biloxi, MS (October 2007)
- Delta Pharma, Inc., Ripley, MS (October 2007)
- Wellness Pharmacy, Birmingham, AL (November 2007)
- Bellevue Pharmacy Solutions, Inc., Saint Louis, MO (November 2007)
- Spoonamore Drug Co., Inc., Louisville, KY (December 2007)

2008

- PharMEDium Services LLC, Cleveland, MS (January 2008)
- AnazaolHealth Corporation, Tampa, FL (May 2008)
- Hopewell Pharmacy and Compounding Center, Hopewell, NJ (June 2008)
- Specialty Pharmacy of Saint Louis, Saint Louis, MO (July 2008)
- National Respiratory Services LLC, Louisville, KY (July 2008)
- Precision Pharmacies, LLC, Bakersfield, CA (August 2008)
- Advanced Physician Solutions, Inc., North Hollywood, CA (August 2008)
- University Pharmacy, Salt Lake City, UT (November 2008)

2009

- Medaus, Inc., Birmingham, AL (February 2009)
- Lee and Company, Inc. dba Lee Pharmacy, Fort Smith, AR (February 2009)
- Prescription Lab Compounding Pharmacy, Tucson, AZ (February 2009)
- Franck's Lab, Inc. dba Franck's Compounding Lab, Ocala, FL (May 2009)
- Franck's Lab, Inc. dba Franck's Compounding Lab, Ocala, FL (June 2009)
- Central Admixture Pharmacy Services, Inc., Chicago, IL (August 2009)
- Franck's Lab, Inc. dba Franck's Compounding Lab, Ocala, FL (December 2009)

2010

- Preckshot Professional Pharmacy, Peoria Hill, IL (June 2010)
- Health & Wellness Compounding Pharmacy, Nashville, TN (August 2010)
- Delta Pharma, Inc., Ripley, MS (September 2010)
- Alwan Pharmacy, Peoria, IL (December 2010)

2011

- Infupharma LLC, Hollywood, FL (September 2011)

2012 (January 2012 through September 25, 2012)

- Weatherford Compounding Pharmacy LLC, Weatherford, TX (February 2012)
- Franck's Lab, Inc. dba Franck's Compounding Lab, Ocala, FL (May 2012)

In addition, between 2002 and October 2012, FDA sought administrative warrants in 25 cases, of which nearly half were for compounding pharmacies. This covers all product areas, not just firms producing drugs. Below are some specific examples of situations in which FDA needed to obtain warrants to inspect compounding pharmacies. Although FDA was ultimately able to obtain warrants to inspect, in many of these cases, the firms' refusals hindered FDA's ability to rapidly investigate reports of serious patient injury including infections and death. This is not an exhaustive list:

Lee Pharmacy (2002)

FDA initiated an inspection of Lee Pharmacy on July 17, 2002, to investigate a complaint from a physician reporting foreign material in a preservative-free sterile injectable drug product made by this firm. Lee Pharmacy's owner refused to provide records, including distribution information identifying consignees of this product, reportedly based on advice from his attorney. Because of these refusals, FDA's inspection ended prematurely on July 18, 2002. FDA attempted another inspection on December 2, 2002, and again was refused. FDA obtained an Administrative Warrant on December 10, 2002, to complete the inspection.

ApothéCure, Inc. (2007)

FDA initiated an inspection of ApothéCure, Inc. on April 26, 2007, to investigate reports of three deaths following administration of injectable colchicine that was later found to be 640 percent superpotent. When the scope of FDA's inspection went beyond the firm's preparation of colchicine, the owner refused to provide records or allow further access to the facility, causing the inspection to conclude prematurely on May 3, 2007. On August 3, 2007, FDA obtained an Administrative Warrant to complete its inspection. FDA's Office of Criminal Investigations investigated the incident and referred the case to the Department of Justice for criminal prosecution. On April 24, 2012, ApothéCure and its owner pleaded guilty to two misdemeanor counts of introducing a drug that was misbranded into interstate commerce.

Health and Wellness Compounding Pharmacy, LLC (2010)

FDA attempted an inspection of Health and Wellness Compounding Pharmacy on April 28, 2010, after learning of a cluster of *Streptococcus endophthalmitis* infections in patients who received injections of Avastin repackaged by this firm. The owner asserted that his firm was not under FDA's jurisdiction and refused to allow FDA to inspect. On August 2, 2010, FDA obtained an Administrative Warrant to inspect the firm.

Infupharma, LLC (2011)

FDA attempted to inspect Infupharma, Inc. beginning on July 18, 2011, after receiving reports of 12 cases of *Streptococcus endophthalmitis* infections following intravitreal injections of repackaged Avastin. After a few days, the owner asserted that his firm was not subject to FDA regulations and, although he agreed to suspend repackaging of Avastin, he would not agree to cease sterile operations. The owner refused FDA access to observe processing of sterile injectable drugs, and, therefore, FDA's inspection ended prematurely on July 22, 2011. After receiving sample analysis

results confirming microbial contamination and information suggesting that Infupharma intended to resume repackaging of Avastin, FDA obtained an Administrative Warrant on September 15, 2011, to complete the inspection and later issued a Warning Letter, citing the firm for adulteration, unapproved drug, and misbranding violations.

Notably, despite recent events, and though we are often working with the state inspectors, our investigators' efforts are being delayed because they are denied full access to records at some of the facilities they are inspecting. For example, during both our recent proactive and for-cause pharmacy compounding inspections, several pharmacies delayed or refused FDA access to records. FDA encountered refusals of at least one FDA request during recent inspections of the following firms and had to seek administrative warrants in two cases as noted:

- Wedgewood Pharmacy, Swedesboro, NJ (November 2012) (obtained warrant)
- JCB Labs, Wichita, KS (February 2013)
- Triangle Compounding Pharmacy, Cary, NC (February 2013)
- University Pharmacy, Salt Lake City, UT (February 2013)
- Avella, Phoenix, AZ (February 2013)
- Foundation Care, Earth City, MO (March 2013)
- Olympia Compounding Pharmacy, Orlando, FL (March 2013) (obtained warrant)
- MedQuest Pharmacy, North Salt Lake, UT (March 2013)
- Pine Pharmacy, Williamsville, NY (July 2013) (obtained warrant)

8. Why does FDA need this authority to effectively regulate compounding pharmacies?

The legal framework at the time of the hearing did not provide FDA with the tools needed to identify and appropriately regulate these pharmacies to help *prevent* product contamination and patient harm. Under section 510 of the FD&C Act, we did not have the authority to require registration of pharmacies that meet certain criteria, so we did not have a list of all of the pharmacies that produce drugs, and we did not know what drugs they are making. While the newly enacted Drug Quality and Security Act (DQSA, P.L. 113-54) provided that outsourcing facilities may register with FDA, the DQSA did not amend section 510. Because of this, our ability to conduct pro-active, risk-based inspections was and remains limited to those pharmacies of which we already had knowledge.

Sometimes we learned about pharmacies because of adverse events or other reports of problems. Our ability to pro-actively apply current good manufacturing practice (CGMP) standards to prevent problems is limited to pharmacies operating more akin to conventional manufacturers, yet our ability to examine records necessary to determine the scope or nature of a compounding operation during an inspection has been disputed. In addition, generally, compounding pharmacies are not required to submit adverse event reports or to label their products with information to help consumers and providers make more informed choices. Since the hearing, the newly enacted DQSA

Page 9 - The Honorable Joseph R. Pitts

when the product is used within a few hours, the risk of patient harm is significantly reduced. If product is shipped interstate, it may be held for a longer period of time before use, with a greater risk of contamination. In addition, there is a risk of inadequate state oversight of the compounding operation, because states have inconsistent standards for sterile compounding and apply varying degrees of resources and expertise to inspections and enforcement. The examples of nine separate incidents, where compounded products caused deaths and serious injuries, described in our testimony of May 23, 2013, illustrate the nature of the risk posed by inadequately controlled sterile compounding operations.

The production of a sterile drug with assured sterility is unavoidably complex, involving multiple steps and manipulations. Controlling the production process to ensure the integrity of the product is even more important when making a sterile product in larger volumes. Each process step could introduce an error or represent an opportunity for the introduction of microbial contamination into the finished product. Under FDA's CGMP regulations, manufacturers of sterile drug products are required to demonstrate that each manufacturing step has been validated to be suitable for achieving and maintaining sterility of the finished drug product, the entire process is performed under extremely high-quality environmental conditions, and there is a high state of control of the entire, integrated process as well as the facility in which sterile drug production is performed. Taken together, these controls result in a high level of assurance that a drug is sterile.

Based on our inspections, FDA learned that compounding pharmacies engaging in sterile compounding often engage in multiple manual manipulations of the product, increasing the risk of contamination. Contamination from operators is one of the more common sources of sterile drug product contamination. Manufacturers of FDA-approved drugs design sterile drug production lines to minimize exposure of the drug product to operators, often relying upon automated equipment that is more reliably sterilized and kept clean, reducing the possibility of contamination.

Considering all of these factors, compounding pharmacies do not have the same high level of sterile drug product quality assurance as manufacturers of FDA-approved drugs.

The Honorable Marsha Blackburn

The response to Question 1 below was e-mailed to Representative Blackburn's Health Policy Analyst on August 8, 2013.

1. **On the ANDAs, you said you prioritize those applications. How long does it take to get one of those through the process? Please elaborate.**

When a complete Abbreviated New Drug Application (ANDA) is submitted to FDA, it takes an average of three months to review it and take action.

Since the enactment of the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012, FDA has expedited the review of 44 ANDAs that have the potential to mitigate a drug shortage. Of those 44 ANDAs, seven included the components required to be considered complete and have actions associated with them. An action is either an "Approval," in which an approval letter is issued, granting the applicant permission to market the drug, or a "Complete Response," in which a complete response letter, or CR, is issued to the applicant, outlining the reasons why an ANDA cannot be approved in its present form. A CR provides information that an applicant can use to re-apply, but is considered a final action. Of the seven complete ANDAs that were expedited, two were approved, and five received CR letters.

Of the remaining 37 ANDAs expedited since FDASIA's enactment:

- Eight are for drugs that were recently added to the drug shortage list and are, therefore, newly expedited. These ANDAs are currently under review.
- Twenty-two will not be approved in their present form. The applicants will receive CR letters when all sections of the application are reviewed, so that all comments can be consolidated into one letter.
- Seven have received and submitted responses to FDA's CR letter, and their newly submitted information is under review.

More information on the ANDA approval process is available at

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm>.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS
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House of Representatives
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August 13, 2013

Dr. B. Douglas Hoey, RPh, MBA
Chief Executive Officer
National Community Pharmacists Association
100 Daingerfield Road
Alexandria, VA 22314

Dear Dr. Hoey:

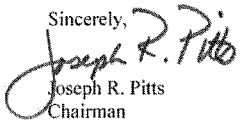
Thank you for appearing before the Subcommittee on Health on Tuesday, July 16, 2013, to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

Also attached are Member requests made during the hearing. The format of your responses to these requests should follow the same format as your responses to the additional questions for the record.

To facilitate the printing of the hearing record, please respond to these questions and requests by the close of business on Tuesday, August 27, 2013. Your responses should be mailed to Sydne Harwick, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Sydne.Harwick@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachments



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August 27, 2013

The Honorable Joseph R. Pitts
Chairman, Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives
2125 Rayburn HOB
Washington, DC 20515-6115

RE: Responses to Questions for the Record for the Subcommittee on Health's Hearing on "Reforming the Drug Compounding Regulatory Framework"

Dear Chairman Pitts:

The National Community Pharmacists Association (NCPA) greatly appreciates the opportunity to respond to the Questions for the Record submitted by Members in response to the Subcommittee on Health Hearing on "Reforming the Drug Compounding Regulatory Framework."

NCPA represents the interests of America's community pharmacists, including the small business owners of more than 23,000 independent community pharmacies. According to a NCPA member survey, almost 86% of independent community pharmacies compound medications. As NCPA stated within its testimony, NCPA commends Members of this Committee for taking a closer look at what actions and inactions led to the tragic NECC event.

The Honorable Henry A. Waxman

AHSP has indicated that hospitals have come to rely on outsourcers to produce large amounts of certain specialized sterile products that are not commercially available. Can you explain what factors might have kept drug manufacturers from manufacturing these products? If outsourcers were unable or unwilling to make these specialized, non-commercially available products, do you believe your members would begin to do so?

NCPA's Response:

According to a recent OIG report entitled, *High-Risk Compounded Sterile Preparations and Outsourcing by Hospitals That Use Them* (OEI-01-13-00150), 56% of hospitals have already made changes regarding outsourcing practices or plan to make changes following the meningitis outbreak including decreasing outsourcing (78.3%) and increasing the hospital's capacity to compound onsite (51.9%). Thus, hospitals are drastically ramping up efforts to compound onsite. Alarming, contrary to the drastic increase in hospitals compounding onsite, this report found that only 56% of hospitals have USP 797-compliant clean rooms for preparing



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sterile compounded medications. This is very alarming where the report found that over half of all hospitals made changes or plan to make changes in order to drastically increase onsite compounding efforts. In fact, the report found that of the hospitals that have already taken steps to ramp up their own onsite compounding efforts, 78% have already decreased outsourcing of compounding and almost 52% have already increased the hospital's capacity to produce sterile compounded medications onsite. Furthermore, the report found that becoming USP-797 compliant might be "resource intensive for hospitals." Specifically, almost 50% of hospitals ranked cost and space limitations as major challenges to USP 797 compliance. Also alarming is the fact that some hospitals were reported as stating that in order to comply with 797, hospitals would have to undergo a building redesign or new construction.

While NCPA would hate to guess as to whether health entities intend to continue to outsource compounding, from the OIG report, hospitals appear to be drastically ramping up efforts to compound onsite instead of outsourcing even where hospitals are not USP 797-compliant. As such, NCPA has expressed strong opposition to exempting any health entities from compounding quality standards as such exemption does not serve the overall goal of providing safe compounded medications to all patients. It should be the intent to ensure all patients receive safe and quality compounded medications regardless of whether the patient seeks such compounded medications from pharmacies within health systems or other compounding pharmacies.

NCPA would encourage the Committee to analyze the main reason that hospitals cited for outsourcing in the first place. According to the same OIG study, 68% of hospitals are forced to outsource due to shortages of commercial products. In fact several of the hospitals sampled in the report stated they outsource only when commercial products are unavailable due to drug shortages and the cost of producing the compounded medication onsite "would be prohibitive." The OIG report goes on to state that "one pharmacy director stated that his hospital had outsourced more CSPs in 2012 than in previous years because of growing shortages of commercially available products." Out of these hospitals that outsourced due to drug shortages, 11% stated that a shortage of outsourced compounded medications would have a life-threatening impact on care in their hospitals.

Drug shortages have long been cited as the reason behind increased compounding efforts and now hospitals are also stating that they feel forced to outsource compounding efforts due to skyrocketing drug shortages. Despite NCPA bringing this to FDA's attention countless times, State Boards of Pharmacy continuing to warn FDA that drug shortages must first be addressed before compounding can be addressed, and hospitals stating that the source of their increased outsourcing is due to drug shortages, FDA has not taken steps to adequately address drug shortages.



The Honorable Cathy McMorris Rodgers

It is my understanding that many of your small business owner pharmacies might only compound 4-6 prescriptions per day. If that's accurate, why has your association been consistently involved as Congress continues to debate a legislative response to the tragic meningitis outbreak?

NCPA's Response:

NCPA represents the interests of pharmacist owners, managers, and employees of more than 23,000 independent community pharmacies across the United States. Independent community pharmacies dispense approximately 40% of the nation's retail prescription drugs, and according to a recent survey, almost 86% of independent community pharmacist's compound. For 34% of those community pharmacists, compounded medications make up less than 1% of their annual dispensed prescriptions. Even though small business owner pharmacies only compound an average of between 4-6 prescriptions per day, the existing legislation could have acute and long term impact on the FDA being granted unprecedented oversight over the practice of pharmacy. Importantly, our members perform a wide variety of compounding services including hormone replacement medications, flavoring medications for pediatric patients, progesterone suppositories to prevent miscarriages, and medications for cystic fibrosis patients, to name a few.

Through compounding, pharmacists can meet the needs of millions of adults, children, and animals. Millions of patients have unique health care needs that cannot be met with commercially available drugs and devices, which might not be appropriate for a particular patient's condition, or simply difficult for a particular patient to consume. Compounding allows these patients to have access to vital medications.

Working with a physician, compounding allows the prescriber and pharmacist to decide a proper course of therapy for each patient by providing customized prescription medication treatments for individual patient needs. Traditional pharmacy compounding offers many benefits, including improving health outcomes and lowering medical costs for patients. In addition, through compounding, community pharmacists provide customized medical treatments, reduce costs while increasing healthy outcomes, and provide patient access to vital medications during times of drug shortages.

While many community pharmacies compound a small amount of medications, the impact of compounding these medications during times of drug shortages can be far-reaching and even lifesaving. When a local VA hospital ran out of potassium chloride and Morphine injections, a local community pharmacist was able to compound these medications and give the VA hospital an emergency supply so that there was not a gap in beneficiary care. In another example, compounding pharmacists provided relief in the nationwide H1N1 outbreak. The nationwide H1N1 (swine flu) outbreak in 2009 led to a rush for Tamiflu in all forms and soon



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there wasn't enough of the liquid version for children. Across the country and with the support of federal health officials and Tamiflu's manufacturer, Roche, compounding pharmacists filled the void and made certain that beneficiaries had access to this vital medication.

Thus, while many community pharmacies compound a small amount of medications, the impact of compounding these medications preserve patient access to vital medications and especially during times of drug shortages, can be far-reaching and even lifesaving.

Some of the legislative proposals I have seen would place burdensome FDA notification requirements on compounding pharmacies in regards to drug shortages. I understand that the response to a drug shortage needs to be nimble and responsive. Do you think that requirements for additional FDA notification would slow the process of providing life- saving medications to patients? If so, how?

NCPA's Response:

In the case of drug shortages, additional FDA notification requirements such as the requirement seen in the Senate legislation that requires the compounder to notify the Secretary within three days from beginning compounding the drug that is in shortage would slow the process of providing life-saving medications to patients. NCPA strongly opposes the requirement that in times of drug shortages the compounder must notify the Secretary when compounding the drug. Not only do compounding pharmacies play an invaluable role in preserving access to compounded medications during times of a drug shortage, compounding is and should remain regulated by state Boards of Pharmacy. Thus, it makes no sense to require compounding pharmacies to notify FDA of their compounding practices, and only serves to decrease access to compounded medications in these already troublesome and ever-growing times of drug shortages.

Compounding pharmacists have filled gaps in the past and should be allowed to continue to fill these gaps in critical times of drug shortages in order to preserve access to medications. As drug shortages continue to skyrocket with little indication that FDA will soon be able to address these shortages, it is irresponsible to the care of patients to require a compounding pharmacy to undertake the timely and burdensome process of notifying FDA when compounding medications in shortage. Furthermore, this additional notification requirement does nothing to prevent another NECC tragedy. At the bare minimum, the requirement of FDA notifications during times of drug shortages should only be placed upon entities defined as "compounding manufacturers" under the legislation.



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The Honorable John D. Dingell

Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies? Please elaborate.

NCPA's Response:

NCPA has always and continues to support clear division between FDA and State Boards of Pharmacy authority when regulating pharmaceutical compounding and manufacturing. NCPA has always believed and advocated that prescription compounding is best regulated by the state Boards of Pharmacy. These state Boards of Pharmacy oversee all aspects of a pharmacy from licensure, oversight of pharmacists and technicians, the process of filling prescriptions, records, documents, and compliance with the state's laws and regulations. Pharmacies are not registered by the FDA and it should remain that way.

Manufacturers, on the other hand, must be registered and regulated by the FDA. We believe that the agency acknowledged that it has the authority to regulate entities like NECC as manufacturers, but just didn't act in a timely manner – whether alone or in concert with the Massachusetts State Board of Registration in Pharmacy – to take appropriate action.

In determining the distinction between pharmaceutical compounding and manufacturing, NCPA has long held that the categories of "pharmacy compounding" and "manufacturing" must be clearly defined and the test to distinguish facilities as manufacturers must be a very targeted approach resulting in a limited number of additional entities determined to be under FDA purview. To the contrary, legislation should not result in broad expansion of FDA power upon the historical oversight by state Boards of Pharmacy of pharmaceutical compounding.

Thus, within the Senate's proposed legislation, NCPA has concerns as to how broad the "test" in determining what is and is not manufacturing will actually reach. The grasp of this "test" is especially alarming in a time when FDA has stated on multiple public occasions including as recent as April 23 at the annual conference of the Food and Drug Law Institute and on April 26 in front of the House of Representatives, that the FDA does not have adequate funds to meet even its current obligations. Specifically, Commissioner Hamburg has stated that "[h]aving adequate resources remains a constant concern." In addition, Commissioner Hamburg has previously reported that FDA will lose an additional \$209 million due to sequestration. Thus, NCPA is concerned that in a time when FDA cannot meet current obligations, it's seeking additional responsibilities.

As such, NCPA would oppose any "test" that results in the expansion of FDA authority over entities that have historically been deemed compounding pharmacies and would like to reiterate the importance that any compounding legislation address the true cause of the NECC tragedy and not result in a method for FDA to gain broad authority over compounding.



Furthermore, any legislative proposal must increase state and Federal communications. More frequent and better quality communication must exist between the state Boards of Pharmacy and the FDA. This should be a bi-communication effort with both the states and the FDA providing more information to work together effectively and efficiently to address all issues that arise and protect all consumers. NCPA strongly urges FDA to share all inspection data in a timely fashion with state Boards of Pharmacy. In addition, FDA should communicate to state Boards of Pharmacy whether the response from the entity addresses all concerns and is sufficient without necessary further action or whether further action is needed from the entity to address these concerns. NCPA also urges the Committee to require FDA to strengthen the communication between its regional offices and the states. In addition, NCPA encourages the Committee to urge FDA to utilize all existing authority and resources in developing and sharing data with states. In order to address the failure in communication by FDA in the past, NCPA would strongly urge FDA to utilize all existing portals and resources in order to produce the needed data sharing to increase communication between the states and FDA.

Does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsourcers and our reliance on them? Please elaborate.

NCPA's Response:

NCPA agrees that while discussing what new regulations should be undertaken to prevent this tragedy in the future, it is also imperative that Congress look at whether current laws and regulations are being properly enforced. It appears from publicly released information that existing Federal and state laws and regulations were not properly enforced with respect to the New England Compounding Center (NECC) operation. It is very important to note that in the case of NECC, many laws and regulations existed at the time of the tragedy that, if enforced, would have severely mitigated or prevented this tragedy.

Massachusetts has state sterility requirements and United States Pharmacopeia (USP) Standard compliance requirements. Massachusetts also has the right to pull a pharmacy's license if that pharmacy is practicing outside the scope of its licensing requirement, and in terms of NECC, publicly available information has shown that the facility was outside the scope of the state's licensure requirements. Therefore, NECC's license should have been pulled long ago had the state properly enforced the regulations and laws already in place. In addition, FDA currently possesses the authority to inspect any pharmacy and to regulate any entity that is operating outside the business of pharmacy as a manufacturer.

In addition, FDA currently has the authority to inspect any pharmacy at any time to assure that the medications stored, inventoried, dispensed, or sold by that pharmacy are safe. The Food, Drug, and Cosmetic Act §704 allows the FDA to inspect "all pertinent equipment, finished and unfinished materials, containers, and labeling therein" of any pharmacy. This same section grants FDA even further authority when the pharmacy is acting as a manufacturer. In



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addition, any pharmacy engaged in the dispensing of controlled substances must also obtain a separate registration from the DEA and is also subject to unannounced inspections of their medications and records by the DEA.

Based on publicly available information, New England Compounding Center was acting as a manufacturer of medications under the guise of a compounding pharmacy. As such, this entity should have been regulated as a manufacturer, not a pharmacy. Even FDA recognized in its 2006 warning letter to NECC, "**Unlike a manufacturer**, you have developed a standardized anesthetic drug product that you sell under the name "Extra Strength Triple Anesthetic Cream". Further, you generate sales by giving physicians 'courtesy prescription' (i.e. free samples). **These actions are not consistent with the traditional practice of pharmacy compounding**, in which pharmacists extemporaneously compound reasonable quantities of drugs upon receipt of valid prescriptions from licensed practitioner to meet the unique medical needs of individual patients."¹

Thank you for the opportunity to submit NCPA's responses for the record, and NCPA looks forward to continuing to work with the Committee to prevent another NECC tragedy while preserving patient access to vital compounded medications.

Sincerely,

A handwritten signature in black ink, appearing to read "B. Douglas Hoey".

B. Douglas Hoey, Pharmacist, MBA

NCPA Chief Executive Officer

¹ See FDA Warning Letters at <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm076196.htm>.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

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August 13, 2013

Dr. Kasey K. Thompson, PharmD, MS
Vice President
Planning and Communication
American Society of Health-System Pharmacists
7272 Wisconsin Avenue
Bethesda, MD 20814

Dear Dr. Thompson:

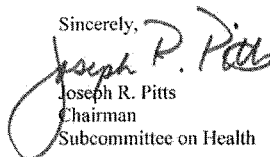
Thank you for appearing before the Subcommittee on Health on Tuesday, July 16, 2013, to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework."

During the hearing, Members asked you to provide additional information for the record, and those requests are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose request you are addressing, (2) the complete text of the request you are addressing in bold, and (3) your response to that request in plain text.

To facilitate the printing of the hearing record, please respond to these questions and requests by the close of business on Tuesday, August 27, 2013. Your responses should be mailed to Sydne Harwick, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Sydne.Harwick@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachment



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Bethesda, Maryland 20814
301-657-3000
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August 27, 2013

The Honorable Joseph R. Pitts
Chairman, Subcommittee on Health
2125 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Pitts,

Thank you for the opportunity to appear before the Subcommittee on Health on Tuesday, July 16, 2013 to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework." During the hearing, Congressman John D. Dingell asked ASHP to provide additional information for the record in the form of three questions. The answers to those questions are provided below.

Again, thank you for the opportunity to provide ASHP's perspective on pharmaceutical compounding and offer potential solutions. We greatly appreciate your leadership on this issue as we work to prevent another tragedy such as the meningitis outbreak of 2012.

Sincerely,

Kasey K. Thompson, Pharm.D., M.S.
Vice President, Policy, Planning and Communication

Cc: The Honorable Frank Pallone, Jr.
Ranking Member, Subcommittee on Health

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Page 2

The Honorable John D. Dingell, questions for the record:

1. Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies? Please elaborate.
2. In your testimony, you mention that your members also use compounded sterile preparations which are not available in an appropriate form from a manufacturer. Is this correct? Would you please submit a list of examples of these kinds of products?
3. Does Section 503(a), as currently drafted and interpreted, recognize the existence of the compounding businesses and our reliance on them? Please elaborate.

Answers:

- 1) Yes, ASHP believes that it is important to have clear lines of regulation between FDA and state boards of pharmacy in order to establish which has authority and accountability for the various entities engaged in compounding. The company responsible for the meningitis outbreak in 2012, the New England Compounding Center (NECC), was licensed by the Massachusetts Board of Registration in Pharmacy as a pharmacy. However, the company was behaving more like a drug manufacturer by preparing sterile medications based on market demand, rather than individual prescriptions and offering them for sale, many times to a customer located in another state. This led to significant confusion among state and federal regulators about who had jurisdiction over NECC, and the manner in which the entity should be regulated (state-required United States Pharmacopeia standards versus FDA-required Current Good Manufacturing Practices). ASHP recognizes that the lines between a traditional pharmacy compounder and an entity operating like a manufacturer may not be clear in all cases, however, we believe that in those questionable or borderline cases, collaboration between state boards of pharmacy and the FDA is necessary to best determine whether or not an entity is no longer operating within the scope of traditional pharmacy compounding. In order to do this the law must be clear that FDA has the authority to make this determination in certain circumstances and to regulate compounding practices that go beyond traditional compounding.
- 2) Our members use compounded sterile medications that are not available in the appropriate form from the manufacturer. Note: Some examples are of sterile injectables prepared according to the manufacturer's instructions, which falls under the USP 797 definition of compounded sterile preparations. However, FDA's current definition excludes this activity from its definition of compounding. The following examples include those not available in commonly used combinations, those requiring further preparation to administer, not available in ready to administer form, and not available at all.

[Document Name]

[Date of Creation]

Page 3

Not available in commonly used combinations

- Preservative free combinations of opioid pain medications with local anesthetics infused with a pump controlled by the patient Intravenous feeding solutions of protein, sugar, electrolytes, vitamins, and minerals
- Mixtures that stop the heart and protect it during cardiac surgery [cardioplegia]

Requires further preparation to administer to patient

- Drugs prepared for administration with specific devices, e.g. intravenous or subcutaneous patient-controlled analgesia pumps, syringe pumps, devices that deliver drugs to the brain [Ommaya reservoir] e.g. pain or anti-spasticity drugs, chemotherapy
- Injectables that are in powder or lyophilized form that require reconstitution or dilution for administration, e.g. common antibiotics, pressor drugs that must be infused slowly, e.g. norepinephrine

Available but not in ready to administer form

- Drugs used in surgery, emergency care, and special procedural areas e.g., interventional radiology and endoscopy not available in pre-filled syringes or ready-to-use infusions, e.g. anesthetics and sedatives
- Drugs not available in the most commonly used dose, e.g. multidose vials of anti-nauseants, pain medications, anesthetics

Not available at all

- Adult drugs used in pediatrics that are too concentrated or need to be preservative-, dye-, alcohol-, or additive-free
- Ophthalmic injections of drugs not labeled for ophthalmic use, but well-studied and reported as safe and effective, e.g. antibiotics, oncologics, and anesthetics.
- Preservative-free versions of drugs for pain, inflammation, and other indications that are injected into the spine or brain

3) ASHP believes that it does not. The marketplace has evolved in such a manner that a new type of pharmaceutical entity has emerged that is neither a drug manufacturer nor a pharmacy. These entities either offer outsourced compounding services or prepare sterile compounded medications without a prescription and offer them for sale to customers, in some cases customers located out of state. Unique preparations and dosage forms for specific patient populations such as pediatrics, efforts to reduce waste of expensive resources, and accreditation requirements have continued to fuel demand for supplies of ready-to-use sterile preparations. Furthermore, current law has been inconsistently interpreted across circuit court jurisdictions. We believe this added to the confusion that occurred over whether states boards of pharmacy or the FDA had authority to regulate the NECC. In short, ASHP believes that current law needs to be updated to reflect this new marketplace, and that Section 503 A does not provide for appropriate regulation of these entities. Because of the lack of clarity in the law, entities such as the NECC were licensed as pharmacies but behaved more like a drug manufacturer. We remained concerned that if this is not addressed events like the fungal meningitis outbreak of 2012 will occur again.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3941

August 13, 2013

Mr. Jeffrey K. Francer
Assistant General Counsel
Pharmaceutical Research and Manufacturers
of America
950 F Street, N.W., Suite 300
Washington, D.C. 20004

Dear Mr. Francer:

Thank you for appearing before the Subcommittee on Health on Tuesday, July 16, 2013, to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework."

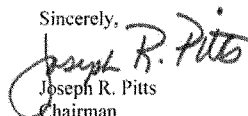
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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachments



950 F STREET, NW, SUITE 300 • WASHINGTON, DC 20004 • 202-835-3400 • PhRMA.org

August 27, 2013

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives
2125 House Rayburn Office Building
Washington, DC 20515

Dear Chairman Pitts:

Thank you for the opportunity to present the views of the Pharmaceutical Research and Manufacturers of America (PhRMA) before the Subcommittee on Health at the hearing entitled “Reforming the Drug Compounding Regulatory Framework” on July 16, 2013. PhRMA is pleased to respond to the questions for the record contained in your letter dated August 13, 2013.

Question from the Honorable Henry A. Waxman

1. **AHSP has indicated that hospitals have come to rely on outsourcers to produce large amounts of certain specialized sterile products that are not commercially available. Can you explain what factors might have kept drug manufacturers from manufacturing these products? If outsourcers were unable or unwilling to make these specialized, non-commercially available products, do you believe your members would begin to do so?**

PhRMA understands from Dr. Kasey Thompson’s testimony on behalf of the American Society of Health-System Pharmacists (AHSP) at the July 16, 2013 hearing entitled “Reforming the Drug Compounding Regulatory Framework” before the Subcommittee on Health that hospitals have served as traditional compounders of sterile preparations that meet patient-specific needs. Both Dr. Thompson’s testimony and studies conducted following the New England Compounding Center tragedy indicate that some hospitals have now outsourced some of this responsibility to large-scale compounding outsourcers. A report published by the Congressional Research Service in June of this year attributed the lack of commercial availability for some of these preparations to factors such as increases in (1) the use of drugs that are dosed by weight, rather than by standardized, commercially available dosing, and (2) the treatment of disorders requiring personalized dosing.¹ Because of the specialized nature of some of these medicines, hospitals and outsourcers engaging in compounding may have been particularly well positioned to fill this need for medicines that require personalized dosing. PhRMA is unable to predict whether its member companies will enter or exit the market for specialized sterile products if outsourcers are unable or unwilling to supply these products. In any event, if large scale outsourcers that act as manufacturers were held to the same standards as NDA or ANDA holders, *hospitals* would continue to be permitted to engage in traditional compounding of sterile preparations – i.e., compounding by a licensed pharmacist or physician pursuant to a valid prescription for an identifiable patient (or, in limited quantities based on a history of prescription orders before the receipt of prescription) under section 503A of the Federal Food, Drug, and Cosmetic Act.

¹ JUDITH M. GLASSGOLD, CONG. RESEARCH SERV., R43082, COMPOUNDED DRUGS 15 (2013).

The Honorable Joseph R. Pitts
 August 27, 2013
 Page 2 of 3

Questions from the Honorable John D. Dingell

1. Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies? Please elaborate.

Yes, PhRMA believes that it is important to have clear lines of division demarcating the appropriate roles of FDA and State boards of pharmacy when it comes to regulating compounding.

In PhRMA's view, the dividing line is and should remain as follows: State boards of pharmacy are responsible for regulating "traditional compounding" (as described in current section 503A of the Federal Food, Drug and Cosmetic Act (FDCA)) under State practice of pharmacy and medicine laws, and FDA is responsible for regulating any medicine prepared outside of traditional compounding, i.e., "non-traditional compounding." In other words, PhRMA believes that State boards of pharmacy should regulate compounding if it involves preparations by either (1) a State-licensed pharmacist in a State-licensed pharmacy, or (2) a State-licensed physician for an identified individual patient that is based on receipt of a valid prescription order or notation and approved by the prescribing practitioner as necessary for the identified patient (or compounded in limited quantities before the receipt of the prescription based on a history of the State licensed pharmacist or State licensed physician receiving valid prescription orders for the compounded drug product). Compounding that does not fit within this definition of "traditional compounding" should be regulated by FDA. For example, any large-scale commercial compounding of prescription medicines should be required to meet the same high FDA standards for drug manufacturers, regardless of whether the commercial producer is designated as a pharmacy or as a manufacturer. These requirements would include, for example, new drug application requirements, compliance with current good manufacturing practices (cGMPs), and risk-based inspections.

PhRMA would support legislation that clarifies the regulatory responsibilities of State boards of pharmacies and FDA with respect to traditional and non-traditional compounding. Specifically, PhRMA would support any clarification that FDA retains its strong existing authority to regulate any medicine compounded outside of traditional compounding as a new drug. PhRMA would also support legislation that includes express inspection and registration authority for non-traditional compounders as manufacturers. This would include, to the extent that such authority is not already clear, the ability of FDA to inspect records to determine whether pharmacies are actually engaging in non-traditional compounding.

Finally, while recognizing the value of having clear lines of division, PhRMA would also support efforts to increase communication and coordination between State boards of pharmacy and FDA relating to compounding issues.

2. Does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsourcers and our reliance on them? Please elaborate.

In PhRMA's view, the Federal Food, Drug and Cosmetic Act (FDCA) currently provides the requisite authority for FDA to regulate a wide range of entities that may engage in compounding, including large-scale compounding outsourcers that may be regulated as pharmaceutical manufacturers. Although as currently drafted, section 503A of the FDCA does not recognize the existence of compounding

The Honorable Joseph R. Pitts
August 27, 2013
Page 3 of 3

outsourcers *per se*, section 503A's intended purpose was never to capture these activities. This section was drafted to create an express exemption for *traditional* compounding pharmacies from the current good manufacturing practice (cGMP) requirements in the FDCA's adulteration provision (501(a)(2)(B)), the adequate direction for use requirement in the FDCA's misbranding provision (502(f)(1)), and the new drug application requirements in FDCA section 505.

In other words, current section 503A exempts from these requirements compounding by a licensed pharmacist or physician pursuant to a valid prescription for an identifiable patient (or, in limited quantities based on a history of prescription orders before the receipt of prescription) *provided* the compounding meets certain other requirements described in 503A. Section 503A's exemption does not apply to non-traditional compounding, i.e., any large-scale commercial compounding by pharmacies or manufacturers that outsource compounded drugs. Such non-traditional compounding may be regulated by FDA under a risk-based approach including, among other things, the FDCA's existing requirements for new drug applications, cGMPs, adequate directions for use, and inspections.

PhRMA's view is that the FDCA currently provides FDA with ample authority to regulate compounding outsourcers. In fact, FDA exercised some of its available enforcement authority in connection with the New England Compounding Center. For example, FDA carried out inspections of compounding pharmacies, worked with state authorities to suspend operations in non-compliant facilities, and arranged for recalls of potentially violative products. PhRMA believes large-scale compounding outsourcers should continue to be regulated under the same risk-based approach as drug manufacturers. To the extent that any clarification is needed, PhRMA would support legislation that clarifies that section 503A creates a limited exemption for traditional compounders, and that all non-traditional compounders (including outsourcers) are—like other drug manufacturing activities—subject to the FDCA's requirements for new drug applications, cGMPs, adequate directions for use, and inspections.

Thank you again for the opportunity to present PhRMA's views on this important public health issue, and please do not hesitate to contact us if we may be of further assistance.

Best regards,



Jeffrey K. Francer
Vice President and Senior Counsel
Biopharmaceutical Regulation

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
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Minority (202) 225-3641

August 13, 2013

Dr. David Gaugh, RPh
Vice President
Regulatory Sciences
Generic Pharmaceutical Association
777 Sixth Street, N.W., Suite 510
Washington, D.C. 20001

Dear Mr. Gaugh:

Thank you for appearing before the Subcommittee on Health on Tuesday, July 16, 2013, to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework."

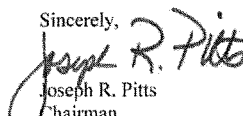
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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachments



August 21, 2013

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
420 Cannon House Office Building
Washington, DC 20515

The Honorable Frank Pallone, Jr.
Ranking Member
Subcommittee on Health
237 Cannon House Office Building
Washington, DC 20515

Dear Chairman Pitts and Ranking Member Pallone,

GPhA would like to submit the following in response to your recent additional questions for the record for the July 16, 2013, hearing before the Subcommittee on Health entitled "Reforming the Drug Compounding Regulatory Framework."

The Honorable Henry A. Waxman

1. **ASHP has indicated that hospitals have come to rely on outsourcers to produce large amounts of certain specialized sterile produces that are not commercially available. Can you explain what factors might have kept drug manufactures from manufacturing these products? If outsourcers were unable or unwilling to make these specialized non-commercially available products, do you believe your members would begin to do so?**

Sterile injectable manufacturing is highly complex, and the products produced require significant science, quality, and regulatory expertise to develop, gain approval from the FDA, and then manufacture and release. Additionally, cGMP standards and Agency regulations, as established by the FDA, require substantial resources. As such, commercially available products must be cost effective for manufacturers to engage in their development, approval, and sustainable manufacturing. Due to the specialized patient needs, some products may not reach the volume required to be cost effective for a pharmaceutical manufacturer to consider as part of its portfolio. In these cases, traditional pharmacy compounding always has and always will play a critical role in patient care. We support the role of the traditional compounders and believe that all patient care needs can be met by the premise of "one patient, one prescription, one drug."

Therefore, while "hospitals have come to rely on outsourcers to produce large amounts of certain specialized sterile produces that are not commercially available," these needs can and should be met by the premise of "one patient, one prescription, one drug."

The Honorable John D. Dingell

- 1. Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies? Please elaborate.**

Yes. GPhA believes that there should be a bright-line standard between traditional compounding and pharmaceutical manufacturing. We believe that if a new category of “compounding manufacturers” is created by legislation, that this legislation should require the “compounding manufacturers” to comply with *all* the same FDA standards that apply to pharmaceutical manufacturers and that the FDA should have full regulatory oversight. This requirement is critically important to ensure the quality and sterility of products and therefore patient safety.

GPhA supports the role of the traditional compounders and believes that compounding pharmacies and pharmacists should compound products only in response to a prescription – one patient, one prescription, one drug. We also believe that oversight of traditional compounders should remain under the oversight of State boards of pharmacy.

- 2. Does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsources and our reliance on them? Please elaborate.**

No. Current law needs to be clarified to ensure the registration, inspection, and proper oversight of “compounding manufacturers.” It should be noted, however, that there are certain complex, high-risk products for which patient safety concerns preclude compounding under any circumstances. Several additional requirements are also needed to ensure the quality and sterility of products and therefore patient safety.

As noted previously, GPhA believes that there should be a bright-line standard between traditional compounding and pharmaceutical manufacturing. Any new category of “compounding manufacturers” should be required to comply with *all* the same FDA standards that apply to pharmaceutical manufacturers, and FDA should have full regulatory oversight.

Additionally, a compounding pharmacy that seeks to “compound manufacture” a copy of a commercially available drug on the drug shortage list should be overseen by the FDA. It should not only have to notify the FDA prior to initiating compounding, but the facility should be inspected by the FDA prior to beginning the compounding of that product. In the interest of protecting public health, the safety and manufacturing standards of compounders producing commercially available products on the drug shortage list should not be lowered below the standards required of pharmaceutical manufacturers.

Requiring the facilities of “compounding manufacturers” to be subject to pre-marketing inspections is paramount to ensuring the quality and sterility of products and therefore patient safety. Given that “compounding manufacturers” must meet cGMP requirements and that building or retrofitting a facility to comply with cGMP requirements will take many months if not years, it would be reasonable to require compounding manufacturers

to notify the FDA of their intentions and be subject to a pre-approval inspection prior to initiating the compounding. Following notification, the FDA should be given the authority to deny a compounding manufacturer's request based on prior risk or other factors. These measures are critically important to ensure the quality and sterility of products and to protect patients.

Thank you again for the opportunity to testify before the Subcommittee.

Sincerely,

A handwritten signature in dark ink, appearing to read 'D. R. Gaugh', written in a cursive style.

David R. Gaugh, R.Ph.
Senior Vice President for Sciences and Regulatory Affairs

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3641

August 13, 2013

Mr. Allan Coukell
Deputy Director
Medical Programs
The Pew Charitable Trusts
901 E Street, N.W.
Washington, D.C. 20004

Dear Mr. Coukell:

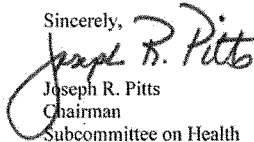
Thank you for appearing before the Subcommittee on Health on Tuesday, July 16, 2013, to testify at the hearing entitled "Reforming the Drug Compounding Regulatory Framework."

During the hearing, Members asked you to provide additional information for the record, and those requests are attached. The format of your responses to these requests should be as follows: (1) the name of the Member whose request you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your response to that request in plain text.

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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachment

**House Committee on Energy and Commerce, Subcommittee on Health, hearing:
“Reforming the Drug Compounding Regulatory Framework”
Questions for the Record from the Honorable John D. Dingell
Response from The Pew Charitable Trusts**

1. Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies? Please elaborate.

To ensure effective regulatory oversight and provide clarity for compounders, it is important to establish which activities are subject to federal regulation. Current law provides neither clarity, nor an effective mechanism for regulation of large-scale compounders whose operations fall far beyond traditional pharmacy practice. Large-scale compounding cannot be addressed simply by asserting these facilities are making unapproved new drugs and requiring them to submit to the New Drug Approval or Abbreviated New Drug Approval process. For example, some large compounders have become a source of intravenous and epidural therapies for hospitals and health systems that do not have the capacity to compound them in-house. Large-scale compounding in anticipation of, or without a prescription is better suited to FDA oversight than to state oversight under current quality standards. However, FDA oversight of compounding need not preclude a facility from maintaining a pharmacy license and carrying out other state-regulated pharmacy practice activities.

2. Does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsourcers and our reliance on them? Please elaborate.

Current Section 503A does not address the existence of compounding “outsourcers”. Modern compounding includes a range of practices, such as preparation of individual doses, small batch compounding of sterile products, and larger batch sterile admixture for hospitals. Under current law, FDA may take action against a compounding facility that is creating unapproved new drugs, but has no ability to conduct routine inspections or enforce quality standards at outsourcers. Congress should update the current regulatory scheme to ensure the appropriate oversight structures and quality standards are in place.

3. Do you believe that simply reinstating Section 503(a) would result in sufficient clarity regarding FDA's authority over compounding pharmacies? Please elaborate.

Varying court rulings have created uncertainty about the status of section 503A. However, merely reinstating section 503A would leave a lack of clarity about which facilities were subject to FDA oversight, and would provide the agency with no way to prospectively identify compounders subject to its jurisdiction, exercise oversight or enforce quality standards. Reinstating 503A would have the practical effect of largely limiting FDA to taking action against compounders only after an adulterated and potentially dangerous drug has been produced and distributed. Congress should explicitly give FDA the tools and authority to hold these facilities to meaningful quality standards in order to prevent drugs from reaching patients.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

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WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3641

August 13, 2013

Dr. David G. Miller, RPh
Executive Vice President and CEO
International Academy of Compounding Pharmacists
1321 Duke Street, Suite 200
Alexandria, VA 22314

Dear Dr. Miller:

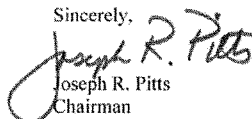
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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachment

Attachment —Member Requests for the Record

During the hearing, Members asked you to provide additional information for the record and you indicated that you would provide that information. For your convenience, descriptions of the requested information are provided below.

The Honorable John D. Dingell

1. Do you believe that it is important to have clear lines of division between FDA and State boards of pharmacy when it comes to regulating compounding pharmacies? Please elaborate.
2. Does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsourcers and our reliance on them? Please elaborate.

FRED UPTON, MICHIGAN
CHAIRMAN

HENRY A. WAXMAN, CALIFORNIA
RANKING MEMBER

ONE HUNDRED THIRTEENTH CONGRESS
Congress of the United States
House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3641

August 13, 2013

Dr. Carmen A. Catizone, RPh, DPh
Executive Director
National Association of Boards of Pharmacy
1600 Feehanville Drive
Mount Prospect, IL 60056

Dear Dr. Catizone:

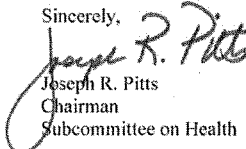
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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Frank Pallone, Jr., Ranking Member, Subcommittee on Health

Attachment

NABP Response to August 13, 2013 Inquiry
July 16th Subcommittee on Health hearing entitled "Reforming the Drug Compounding
Regulatory Framework."
Dr. Carmen Catizone

1. Do you believe that it is important to have clear lines of division between FDA and State Boards of Pharmacy when it comes to regulating compounding pharmacies? Please elaborate.

Yes. NABP has determined, based upon our actual inspection of compounding pharmacies for the states and long involvement in the practice of compounding, that a clear line of division between compounding and manufacturing is absolutely necessary to protect the public health. Absent this division, the ambiguous regulatory environment that would exist and presently exists, allows for entities to manufacture under the guise of compounding with little if any oversight or regulation.

2. Does Section 503(a), as currently drafted and interpreted, recognize the existence of these compounding outsources and our reliance on them? Please elaborate.

The existing language of Section 503(a) does not address compounding outsourcers or their activities in the preparation of drug products. The proposed language of the Senate HELP Bill does define and provide for the regulation of compounding outsourcers.